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Atomic spectrometry update. Clinical and biological materials, foods and beverages

Andrew Taylor,*[a] Simon Branch,[b] David Halls,[c] Marina Patriarca[d] and Mark White[e]

[a]*Supra-regional Assay Service, Trace Element Laboratory, Centre for Clinical Science and Measurement, School of Biomedical and Life Sciences, University of Surrey, Guildford, Surrey, UK GU2 7XH. E-mail: A.Taylor@surrey.ac.uk*
[b]*The Lord Rank Centre, R. H. M. Technology, Lincoln Road, High Wycombe, Buckinghamshire, UK HP12 3QR*
[c]*Trace Element and Micronutrient Unit, Department of Clinical Biochemistry, Glasgow Royal Infirmary University NHS Trust, Castle Street, Glasgow, UK G4 0SF*
[d]*Laboratorio di Biochimica Clinica, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma, Italy*
[e]*Health and Safety Laboratory, Health and Safety Executive, Broad Lane, Sheffield, UK S3 7HQ*

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This ASU reviews publications that appeared in the twelve months up to the end of October 2002. The writers found there to be an interesting collection of publications and enjoyed the opportunity to review current analytical activity for clinical and biological materials, foods and beverages. It was noted that Chinese-based scientists are responsible for much of the innovations that we have reported in this Update. This year has seen tremendous growth in the employment of permanent chemical modifiers for electrothermal atomisers. Rhodium was introduced for the measurement of selenium, just a couple of years ago, and now it is looking as if it may displace palladium as the modifier of choice for this and many other determinations. The writers were impressed by an unusual device that produced a dry 'aerosol', allowing the transfer of solid powdered material into a quartz tube mounted above a flame burner head. As the sample had to be reduced in size to a very fine powder it is unlikely that the technique will gain widespread popularity but the idea in principle appears very clever. Similarly, the use of ICP-mass spectrometry as a measurement technique for immunoassay, while novel, does not appear to be very practical when an assay can involve several hundred measurements. A number of intriguing papers were noted. We were impressed by the subjects who participated in studies of dermal penetration of nickel compounds—these individuals had sticky tape placed on the skin, which was then pulled off together with underlying cells; this procedure was then repeated up to 20 times. We pondered over a method that involved formation of SeH_2, which was oxidised to Se^0 and trapped on a hot gold wire. After a trapping period of up to 5 min the Se^0 was released for hydride formation and measurement. The English expression "takes the biscuit" came to mind as we puzzled with an even more remarkable report of the measurement of iron and manganese in biscuits by a cold vapour technique! After which, the revelation that camels' milk is an ideal nutrient caused barely a second thought.

In response to the need to assure the quality of analytical results and their mutual recognition, standards for the accreditation of analytical laboratories have been developed by ISO and other bodies in recent years. Somewhat earlier there was a revision of the terminology used to describe or characterise analytical methods and performance and also to take into account the "new" concept of "uncertainty of measurement". This terminology also appears in the international standards. Thus, the term "*accuracy*" has been chosen to indicate the closeness of the agreement of an individual result with the "*true*" value of the measurand. It is acknowledged that accuracy cannot be measured, but that the "*uncertainty*" of measurement associated with a result, *i.e.*, the interval of values which can be reasonably attributed to that measurand, may be determined. A new term, "*trueness*", defines the closeness of the agreement of the mean of several results with an assigned value, *e.g.* of a certified reference material, and can be estimated as "*bias*". "*Precision*" is a general term to describe the closeness of the agreement between replicate measurements of the same sample by the same method. However, several different factors may affect estimates of precision and the terms "*repeatability*" and "*reproducibility*" are used to indicate two extreme conditions. Repeatability refers to measurements made under identical conditions, as far as possible (equivalent to within-batch precision). Reproducibility is applied to precision estimates that take account of all possible variables, including laboratories (more or less equivalent to between-laboratory precision). The term "*intermediate precision*" refers to conditions lying between these extremes and it is recommended that the variables (time, operators, equipment, reagents, *etc.*) be indicated. In order to reflect these developments, the authors of this Update intend to adopt the new terminology when commenting on results. However, where work is directly cited we shall use the expressions given by the original workers, to avoid misrepresentation of what was written. This annual review covers the published literature on the analysis of clinical and biological materials, foods and beverages using atomic spectrometric techniques for the year up to October 2002. Tables 1 and 2 summarise details of these publications. Our previous Update[1] covered the twelve months up to October 2001.

1 Analysis of clinical and biological materials

1.1 General reviews and articles

Szpunar and Lobinski[2] described recent research in their laboratory in *speciation analysis of essential and toxic elements in biological systems*. They have gone beyond the simple coupling of HPLC and ICP-MS to a multi-dimensional approach to obtain more information on the species, *e.g.* sequential use of different HPLC separation mechanisms and CE for separation; electrospray MS, including collision induced dissociation MS, for detection.

It is often difficult, or inappropriate, to collect 24 h urine samples for assessment of exposure to toxic elements. *Collection of a random sample and correction by expressing the result as a ratio to creatinine* is the most usual way of getting round this. Is this necessary or reliable, however? The study of Hinwood *et al.*[3] attempted to answer this problem for the measurement of inorganic As in urine in population studies by comparing 160 paired 24 h collections and corresponding first morning void spot samples. For both concentration and creatinine-corrected concentration, there were no significant differences between the urine As in the two types of sample. They concluded that for environmental exposure studies, creatinine adjustment of the concentration of spot samples may not be necessary. However, most of the concentrations measured were very low and it may be unwise to extend this conclusion to higher concentrations found in occupational exposure. They found when they confined the dataset to more measurable concentrations that the relationship between the concentration and the creatinine-corrected concentration became non-significant.

1.2 Sampling and sample preparation

1.2.1 Sample collection and stability. Work by Rodushkin and Odman[4] has confirmed the problems of *contamination of samples with trace elements from blood collection tubes*. They measured 70 elements by magnetic sector ICP-MS in 0.05 M HNO_3 solutions after contact with disposable stainless steel needles, blood collection tubes including separator tubes, disposable plastic pipettes and plastic tubes used for sample storage. For elements normally present in blood or serum at concentrations greater than 10 $\mu g\ l^{-1}$, contamination was generally negligible (*i.e.* less than 1% of expected concentration), but for elements at concentrations less than this, contamination could severely impair accuracy. Commercial blood collection and serum separator tubes were the main problem, especially for Al, Ba, Th and the REEs.

The study of Sabe *et al.*[5] on *the stability of selenium in urine* showed that acidification with HCl had no effect on stability

and that the concentration was stable for 24 h at room temperature, for a week at 4 °C and for 14 days at −20 °C.

1.2.2 Sample preconcentration. An on-line system for preconcentration of Gd in digested urine using FI and ICP-AES was reported by Ortega *et al.*[6] This novel approach used *cloud-point extraction* of a complex of Gd^{III} with 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol formed in the presence of non-ionic micelles of PONPE-7.5 at a thermostatted temperature of 25 °C, above the cloud-point temperature of the system. The surfactant-rich phase of this system was retained on a micro-column packed with cotton. The Gd was eluted with 4 M HNO_3 into the nebuliser of the plasma. With 10 ml of sample solution, an enrichment factor of 20 was attained, giving an LOD of 40 ng l^{-1}. Normal Gd concentrations in six urines ranged from 0.25 to 0.52 μg l^{-1}.

For the determination of Pd in human urine by ETAAS, Costa *et al.*[7] developed *a sequential system using preconcentration* after reacting the Pd with NaDDC to form a complex which was retained on a column of silica C_{18}. This was eluted with about 43 μl of CH_3OH directly into the graphite furnace. With a sample of 8 ml of urine, an LOD of 8 ng l^{-1} could be reached and analyses could be made at the rate of 10 samples h^{-1}.

Polyurethane foam, ground down to a 1 mm diameter pore size, quantitatively extracts Co as a thiocyanate complex in 0.1 M HCl, as reported by Sant' Ana *et al.*[8] They used this to preconcentrate Co by a factor of 10, achieving an LOD of 0.08 μg l^{-1}. The foam was filtered off, dried and injected as a solid into a graphite furnace for determination by ETAAS. The foam was removed by pyrolysis at 550 °C and calibration could be made with aqueous standards. This approach was used to determine Co in digested marine biological CRMs with good results.

1.3 Developments in and applications of multi-element techniques

1.3.1 Atomic emission spectrometry with the inductively coupled plasma and the microwave induced plasma. Tohno *et al.* have continued their studies on *calcification of tissues in ageing* using ICP-AES to measure Ca, Mg and P. Results on 24 Japanese subjects aged between 65 and 93 y[9] showed an accumulation of these elements in the iliac arteries, with significant correlations between all three elements. The mass ratios of Mg to Ca and Mg to P were lower at advanced accumulation than at the early stage. Significant correlations were also found between the concentrations of all three elements in Japanese monkey arteries.[10] To see whether the conclusions that they had reached on studies of Japanese subjects were the same for other races, they measured Ca, Mg and P in the arteries of 16 Thai subjects.[11] Magnesium increased in the arteries with ageing, paralleling the increases in Ca and P.

Whereas the elderly suffer from the build-up of Ca, Mg and P, the infant has problems in getting enough of these elements. *Balance studies for calcium, magnesium and phosphorus on ten extremely low birthweight infants* were carried out by Loui *et al.*[12] using ICP-AES measurements. They concluded that these infants have high nutritional needs for Ca, Mg and P which are not met by a human milk fortifier widely used in Europe.

Matrix effects in the determination of calcium, potassium, magnesium and sodium in urine by ICP-AES were investigated by Krejcova *et al.*[13] Whereas K and Na could be determined directly in undiluted urine, for Ca and Mg a suppression interference was found which was overcome by matrix-matched calibration and internal standardisation.

An *on-line flow system for preconcentration* was developed by Menegario and Gine[14] for the determination of Cd, Cu, Mn, Ni and Pb in saliva samples by ICP-AES. Saliva (1 ml) was passed through a microcolumn containing 8 μl of AGSOW-X8 resin. The elements were eluted with 3 M HCl at 82 μl min^{-1} into a microconcentric nebuliser. Enrichment factors ranged from 17 to 46.

To measure *boron in blood* of patients treated with the agent 4-dihydroxyborylphenylalanine (BPA) during neutron-capture therapy, Laakso *et al.*[15] found that measurement by ICP-AES had distinct advantages over the use of ICP-MS. The well-established ICP-MS procedure was tedious because prior wet ashing was necessary. For ICP-AES, sample preparation could be simplified to protein precipitation with TCA. Red cell B concentrations were calculated from the measurements of plasma and whole blood B and the blood haematocrit. The method was shown to be precise (RSD within- and between-batch < 5%), accurate (recoveries in whole blood 95.6–96.2%) and to give results which correlated well with those obtained by ICP-MS (r = 0.994).

Electrothermal vaporisation was applied by Chen *et al.*[16] to the analysis of small volumes of both solid and fluid biological samples by ICP-AES. By adding a PTFE slurry to the sample to generate F, matrix effects were reduced considerably. The method was applied to the analysis of human hair slurried after partial digestion with a small volume of HNO_3, a slurry of Chinese medicine powder and serum samples. The precision was in the range 2–4% RSD and LODs were 11, 1.2, 2.0, 2.5, 1.0 and 242 μg l^{-1} for Ca, Cu, Cr, Fe, Ti and Zn, respectively.

For a study of *gallstone formation in humans*, Szentmihalyi *et al.*[17] measured concentrations of 23 elements in bile fluid and gallstones by ICP-AES. Samples were microwave digested with HNO_3–H_2O_2 in Teflon vessels. Significant correlations were found between the element pairs Al–Ca, P–Mg and S–Mg in bile and Al–Ca, Mn–Ca, Mn–Al in gallstones. Concentrations of Al, Ca, Cr, Cu and Mn were found to be 120–360-fold higher than in bile. They concluded that Cr and Mn in bile had an effect on Ca and Al precipitation in gallstones.

Inductively-coupled plasma AES is a very suitable technique for *the simultaneous determination of elements in tissue samples*. In a study of brain tissue from a patient who died with Wilson's disease, Faa *et al.*[18] found that not only were the Cu concentrations higher than normal, as expected, but the concentrations of Ca, Fe, Mg, P, S and Zn were considerably lower than normal. The elements were distributed unevenly throughout the brain. Correlations of trace element concentrations within and between six different autopsy tissues were studied by Rahil-Khazen *et al.*[19] Thirteen elements were measured by ICP-AES. They found that Fe–Co were correlated in most tissues and that Cd–Zn, Cu–Mn, Cu–Zn and Mn–Zn were highly correlated in the kidney medulla. Many more correlations were found and the authors expected that this would help in an understanding of the kinetic interactions of trace elements in the body. Their further analysis of the data[20] showed that in most tissues the concentrations of the essential elements followed the order Fe > Zn > Cu > Mn > Se > Cr > Co, except in the ovary where Se was higher than Mn. Generally, males had higher concentrations of trace elements in tissues, but females had higher Mn in the brain front-lobe and heart and Sr in the liver. Accumulation of Ba and Sr with age was evident in most tissues with Al accumulating in the kidney cortex and Cd in the brain cerebellum. A similar study, mainly on toxic elements, was reported by Yoo *et al.*[21] on Korean subjects. They found that Cd accumulated with age in the liver, kidney, heart and testis and Pb accumulated in the testis and bone. The elements Hg, Se and Zn were not correlated with age in any tissue. Correlations were seen between the element pairs Hg–Se, Pb–Se and Cd–Zn in many tissues.

1.3.2 Inductively coupled plasma mass spectrometry and other mass spectrometric techniques. *1.3.2.1 Multielement determination by ICP-MS.* Reference values *for 13 elements in whole*

blood and serum from 15-year old Swedish adolescents were carried out by Barany et al.[22] The samples from 372 subjects, measured by ICP-MS, gave median concentrations of Cd, Pd, Pt, Rh, Tl and W below the LOD of the technique and median concentrations of Co, Cu, Se and Zn in agreement with values from other studies, but median concentrations of Cd, Hg and Pb were lower. Concentrations in serum showed significant correlation to values in whole blood for the elements Co, Cu, Hg, Pb, Rb, Se and Zn. Dombovari *et al.*[23] reported reference values for 12 elements in the serum of young Hungarian adults of mean age 22 y. Most elements were determined after microwave digestion with HNO_3–H_2O_2, but as the blanks for Al were too high, a separate digestion with TMAH was made for that element. Tissue trace element concentrations were reported by Garcia *et al.*[24] for 78 non-occupationally exposed subjects from Tarragona in Spain. For lung, liver, kidney, brain and bone, concentrations of As, Co, Cr, Hg and V were near or below the LOD of ICP-MS. Concentrations of Mn, Sn and Zn were similar to those reported in other studies, but concentrations of Cd, Ni and Pb were lower and Cu was higher. No obvious hazard from environmental exposure or from diet was evident for people living in the study area.

An interesting *in vitro* study on *the release of toxic elements from button batteries* was reported by Rebhandl *et al.*[25] Twenty elements released from eight different types of button cells into simulated gastric juice were measured by ICP-MS. Within 4 h, leakage was seen from almost all batteries with the release of significant amounts of Cd, Hg and Pb. Between 24 h and 72 h, dissolution, holes and defragmentation were seen and the authors considered that the current policy of conservative management of batteries lodged in the stomach should be reassessed.

For a study of *trace element changes in aortic valve sclerosis*, Nystrom-Rosander *et al.*[26] measured 15 elements by ICP-MS in sclerotic valves taken from 46 patients undergoing surgical aortic valve replacement. Comparison was made with 15 forensic autopsy samples from individuals with no known cardiac disease. The most pronounced increases in the sclerotic valves were for As (5-fold), Ca (70-fold), Co (10-fold), Fe (20-fold), Mg (20-fold), Pb (8-fold) and Zn (10-fold). A smaller increase was seen for Cd and decreases in Cu, Se and V were found.

1.3.2.2 Sector field ICP-MS (SF-ICP-MS). In a comparison of SF-ICP-MS with quadrupole ICP-MS for the determination of ^{232}Th, ^{235}U and ^{238}U in urine, Pappas *et al.*[27] found that the sample volume could be reduced from 500 µl to 100 µl for the more sensitive sector-field method while still getting a small improvement in LOD to less than 3 ng l^{-1}. In their approach, Truscott *et al.*[28] used on-line high-performance chelation IC to remove spectral interferences in the determination of Np, Pu, Th and U by SF-ICP-MS. Different oxidation states of Np, Pu and U were also evident in the separation. The method was evaluated by determination of ^{239}Pu in NIST Human Lung SRM with results within the certified range.

Reference values for 14 trace and ultra-trace elements in the serum of 59 healthy subjects were reported by Muniz *et al.*[29] Measurements were by SF-ICP-MS after dilution 1 + 4 with ultrapure H_2O using added Ga, Sc, Tl and Y as internal standards. Measurements of the same elements in 14 samples from haemodialysis patients showed higher Al, Co, Cr, Cu, Mn, Mo, Pb, Sr and U concentrations and lower levels of Fe, Rb and Zn.

To study *species of arsenic, antimony, germanium, mercury, selenium and tin excreted in urine after fish consumption*, Kresimon *et al.*[30] derivatised the species by reduction with $NaBH_4$, separated them by low-temperature GC and detected the elements by ICP-MS. In this way, they could detect seven As, two Ge, one Hg, five Sb, three Se and four Sn species. Of these 22 species, 18 were identified.

Sturup[31] developed a new method for *the determination of calcium isotope ratios* and total Ca using SF-ICP-MS with a shielded torch. The isotope ratios ^{44}Ca:^{43}Ca, ^{42}Ca:^{43}Ca and ^{44}Ca:^{42}Ca could be measured in urine with precisions of 0.25, 0.23 and 0.05% RSD, respectively, in order to determine the Ca absorption from various foods. Uncertainty calculations showed that when enriched stable ^{44}Ca and ^{42}Ca are given in double stable isotope procedures, the overall uncertainty is limited by the precision of the ICP-MS measurements of the ^{44}Ca:^{43}Ca and ^{42}Ca:^{43}Ca isotope ratios.

1.3.2.3 The dynamic reaction cell in ICP-MS. There are still very few publications that have appeared on *applications of the dynamic reaction cell to the analysis of clinical and biological materials.* Chang and Jiang[32] showed that NH_3 in a dynamic reaction cell effectively reduced isobaric interferences by 2–3 orders of magnitude in the determination of Cr in water and urine. Results on SRMs for both water and urine agreed well with the certified values.

1.3.2.4 Speciation with capillary electrophoresis coupled to ICP-MS. Sanz-Medel's group in Oviedo, Spain, have been exploring the potential of capillary electrophoresis coupled to inductively coupled plasma mass spectrometry. For speciation of Hg, inorganic Hg and alkylmercury compounds were converted to complexes with cysteine which were separated by CE in an $Na_2B_4O_7$ buffer at pH 9.3, converted to volatile species by reduction with $NaBH_4$ and the Hg detected by ICP-MS. The use of the volatile species generator overcame problems related to the direct connection of CE to a nebuliser and also gave improved LODs (1 µg l^{-1} for inorganic Hg and 30 µg l^{-1} for methylmercury). The technique was evaluated on the determination of methylmercury in the dogfish liver CRM DOLT-2 with a satisfactory result. For the separation of metallothioneins in rabbit liver,[33] they used UV detection to establish suitable conditions for separation by CE. Coupling of CE to ICP-MS then allowed metal speciation. A comparison of Meinhard, Babington and high-efficiency nebulisers for coupling to CE was made.

1.3.2.5 Laser ablation ICP-MS. Feldmann *et al.*[34] have shown that problems *in the analysis of thin sections of tissue by laser ablation* can be overcome by keeping the sample frozen at temperatures below −60 °C. Their cryogenically cooled ablation cell was coupled to an ICP-TOF mass spectrometer. With the use of ^{13}C as an internal standard to compensate for fluctuations in ablated material, reproducibilities of 2–6% RSD were achieved. Calibration was achieved with a pressed and frozen slice of Pig Liver CRM, which was shown to be suitable for a range of kidney and liver samples. The method was seen as offering the possibility of 2-dimensional analysis of trace elements in tissue samples with a resolution of better than 20 µm.

1.3.2.6 Accelerator mass spectrometry. Jackson *et al.*[35] have reviewed *the application of accelerator mass spectrometry for studies on nutrition* using the isotopes ^{14}C, ^{26}Al and ^{41}Ca. The technique offers the advantages of small doses that present no health risk, high sensitivity, small sample size and the possibility of making measurements over a long time.

Results obtained by Yokel *et al.*[36] showed that a small *fraction of aluminium that has been absorbed* reaches the brain where it persists for a long time. Their study used AMS to measure ^{26}Al in rats injected with Al transferrin or with Al citrate spiked with ^{26}Al. Irrespective of the form of Al, about 0.005% of the ^{26}Al reached the brain, decreasing with a half-life of about 150 d. With desferrioxamine treatment, the half-life reduced to 55 d.

1.3.2.7 Resonance ionization mass spectrometry. Resonance ionization mass spectrometry has been applied by Blaum *et al.*[37] to the determination of Gd in the tissues of mice injected with Gd diethylenetriaminepentaacetic acid, a contrast agent used for magnetic resonance imaging (MRI). Using a three-step resonant excitation step into an autoionizing level, it was possible to determine down to 1.6 pg Gd with a linear response over six orders of magnitude. Measured concentrations in the tissues ranged over two orders of magnitude.

1.3.2.8 Secondary ion mass spectrometry. The location of *elements in the goblet cells of rat conjunctiva* was studied by Oba *et al.*[38] using SIMS and results were compared with those obtained with EDXRF. With an O_2^+ primary ion source, SIMS showed good resolution of Ca, K, Mg and Na as positive ions and with a Ga^+ ion source, Cl, CN, OH, P and S as negative ions. The elements Ca, C, Cl, K, Mg, Na, N, O, P and S were shown by EDXRF with poorer resolution.

1.3.3. X-ray fluorescence spectrometry. *1.3.3.1. Elemental mapping.* Studies using elemental mapping have highlighted some *of the changes in trace element concentrations that occur in cancerous tissue.* Copper, Fe and Zn in a total of 80 cancerous and healthy breast tissue samples were examined by Geraki *et al.*[39] using SRXRF. All three elements were increased in the tumours, Cu by an average of 3.6-fold, Fe by 2.7-fold and Zn by 4.4-fold. The distribution of Zn in normal and cancerous human prostate tissue was quantified by Ide-Ektessabi *et al.*[40] using SRXRF. In normal tissues, concentrations of 101–180 $\mu g\ g^{-1}$ were found in the stroma and 158–474 $\mu g\ g^{-1}$ in the epithelial cells. In cancerous cells, the range was 44–713 $\mu g\ g^{-1}$ in the stroma and 89–221 $\mu g\ g^{-1}$ in the adenocarcinoma.

Mapping can give information at the cellular level and this has been used to study *changes in neurological diseases.* Distribution of Fe in nerve cells of a patient with Parkinsonism–dementia complex was evaluated by Ide-Ektessabi *et al.*[41] using XRF and Fe K-edge X-ray absorption near-edge structure spectroscopy. Iron was concentrated in the neuromelanin granules and in one of the glial cells surrounding the neuromelanin granules. Chemical state imaging showed that the Fe in the glial cells was mainly as Fe^{3+}, while in the neuromelanin granules, it was as both Fe^{2+} and Fe^{3+}. In a study of senile plaques in Alzheimer's disease, Robertson *et al.*[42] used micro-PIXE measurements to show that the concentration of Zn was higher in the senile plaques than in the adjacent neutrophils and that the Zn in these neutrophils was higher than in control neutrophils. They suggested that in Alzheimer's disease the delicate balance of brain Zn is disrupted and this could play a role in neuron degeneration.

The fate of *toxic elements in respired particles* was studied by Pinheiro *et al.*[43] Thin frozen sections of lung tissue were examined by micro-PIXE. Significant particle deposits were found at the distal respiratory tract containing the elements Al, Cr, Cu, Fe, Ni, Si, Ti, V and Zn. The pattern of mobilisation of elements from these deposits to the surrounding tissue was different in the respiratory tract and in the respiratory ducts. The elements Ni and V showed evidence of high solubility.

Mapping of chromium in the testicular tissue of mice injected with $CrCl_3$ was carried out by Ortega *et al.*[44] using XRF with proton and SR beams. The average Cr concentration was about 5 $\mu g\ g^{-1}$ but higher concentrations were found within the limiting membrane of the testes, the tunica albuginea. The superior resolution of SRXRF allowed Cr to be seen also within isolated cells from the interstitial connective tissue.

1.3.3.2 Fundamental developments in in vivo XRF determination of lead in bone. Todd[45] has reviewed *theoretical considerations in the* in vivo *measurement of lead in bone* by L-shell XRF. The review covers the method of correcting for attenuation, the contributions to the measurement uncertainty, interferences, the depth of bone sampled and the signal strength. In a further paper,[46] he reported on the development of an L-shell XRF bone Pb measurement system. A secondary target gave greater Pb X-ray signal-to-background ratios than partially plane polarized XRF. Calcium in the matrix reduced the signal substantially and attenuation by skin and adipose tissue had a profound effect. Kondrashov and Rothenburg[47] described mathematical techniques for uncertainty calculations for *in vivo* measurement of Pb in bone by XRF using a ^{109}Cd source.

There has been some interesting work on establishing *the accuracy and precision of* in vivo *bone lead measurement.* Todd and collaborators compared results by XRF with those by ETAAS after ashing and dissolution in HNO_3. In measurements on the femurs of pigs,[48] concentrations of Pb ranged from 1.0 to 24.5 $\mu g\ g^{-1}$ by ETAAS. On average, XRF overestimated Pb measurement by 2.6 $\mu g\ g^{-1}$, which was 2 $\mu g\ g^{-1}$ poorer than had been observed in studies of human tibiae. They concluded that measurements of Pb in non-human bones by XRF may require adjustment of the XRF spectrum peak extraction method. The variability of measured Pb concentrations in nine adult human tibia was also studied.[49,50] Using ETAAS measurements, they established that the surface tibia Pb concentration was greater than the core concentration by about 5–8 $\mu g\ g^{-1}$. Both core and surface tibia Pb concentrations were lower at the proximal and distal ends of the tibia. With ^{109}Cd-based K-shell XRF measurement, the opposite had been found. Results obtained by XRF showed no significant difference from results obtained by ETAAS on surface Pb, but XRF significantly overestimated the tibia core Pb concentration by around 5–8 $\mu g\ g^{-1}$. In a further study evaluating L-shell XRF measurement,[51] the difference between measurement on intact legs and on bare tibiae was assessed using adult human cadavers. Agreement between XRF and ETAAS measurement was reasonably good for bare bone measurement, but poor for intact leg measurement. The authors concluded that the variability of the L-shell XRF measurement was large enough for both bare bone and intact leg measurements to give grave concern about the analytical use of the technique *in vivo*.

1.3.3.3 Applications of in vivo XRF determination of lead in bone. Gerr *et al.*[52] found that substantial *lead exposure during childhood* could increase blood pressure during young adulthood. Lead exposure was assessed by *in vivo* XRF measurement of the bone Pb of 508 participants. Results were divided into 4 groups according to bone Pb concentration. The group with the highest bone Pb ($> 10\ \mu g\ g^{-1}$) had an average diastolic blood pressure 2.3 mm Hg higher than those in the lowest bone Pb group ($< 1\ \mu g\ g^{-1}$).

In a study of *the impact of breastfeeding on the mobilisation of lead from bone*, Tellez-Rojo *et al.*[53] measured *in vivo* bone Pb at one month *postpartum* on 425 lactating women in Mexico City. Blood Pb was measured at 0, 1, 4 and 7 months *postpartum*. Mean blood Pb at delivery was 84 $\mu g\ l^{-1}$ (0.41 $\mu mol\ l^{-1}$) and cortical and trabecular bone Pb were 10.6 and 15.3 $\mu g\ g^{-1}$, respectively. Women who exclusively breastfed their infants showed a mean increase in blood Pb of 14 $\mu g\ l^{-1}$ (0.07 $\mu mol\ l^{-1}$) and those that practised mixed feeding increased by 10 $\mu g\ l^{-1}$ (0.05 $\mu mol\ l^{-1}$).

The normative aging study in the USA has provided much information about *the fate of lead in bone.* Bone and blood Pb concentrations in 656 middle-aged and elderly men were related to previous occupational history in a study reported by Elmarsafawy *et al.*[54] None had worked in the primary lead industry and they were divided into blue-collar (BC) and white-collar (WC) occupations. The tibia and patella Pb concentrations of BC workers were on average 5.5 and 6.5 $\mu g\ g^{-1}$ higher, respectively, than those of the WC subjects. Non-white BC workers had even higher bone Pb concentrations than their

white colleagues. Data from this study has also been used to assess the influence of bone resorption on Pb mobilization by Tsaih *et al.*[55] Bone resorption was assessed on 333 men by measuring cross-linked *N*-telopeptides of type 1 collagen in 24 h urine collections by immunoassay. Blood and urine Pb were measured by ETAAS and ICP-MS, respectively. After adjustment for age and creatinine clearance, an association between urinary Pb and patella Pb was found which was more pronounced in the groups with higher indices of bone resorption. A similar association was found for blood Pb and patella Pb, confirming that bone resorption influences the release of Pb from bone stores into the circulation. Results from the same research group on middle-aged and elderly women[56] indicated a significant association between postmenopausal oestrogen levels and blood Pb. Bone Pb was significantly correlated to blood Pb but only for postmenopausal women not taking oestrogen. The results suggest that increased bone resorption, as occurs postmenopause because of decreased oestrogen production, results in increased release of Pb from bone.

1.3.3.4 Determination of elements in body fluids by XRF. Total reflection X-ray fluorescence is showing its potential in the multielement analysis of human body fluids. In serum, the high organic content increases the background due to Compton scattering. Zarkadas *et al.*[57] showed that a molybdenum filter inserted after the cut-off reflector significantly improved the peak-to-background ratio, especially for Br, Cu, Se and Zn. They could determine these elements with a precision of about 4% RSD. In their method, Marco *et al.*[58] used the Compton peak as an internal standard in the determination of Cu, Se and Zn in serum. Reference values on healthy subjects were established based on age and sex. From their results on cancer patients, which were significantly different from normal, they suggested that the Zn : Cu ratio and the Cu concentration could be a useful tool for cancer diagnosis. However, these authors should note that the changes in serum Cu and Zn which they observed are not specific to cancer, which would make it a poor diagnostic tool. Amniotic fluid samples were analysed by Carvalho *et al.*[59] by TRXRF. The organic matrix was removed by treatment with HNO_3 followed by O_2 plasma ashing. Yttrium was added as internal standard. Placenta samples were lyophilised and analysed by EDXRF. Only two elements measured, Ca and Fe, showed a relationship to the mother's age and the weight of the newborn. Calcium in both amniotic fluid and placenta increased in heavier babies and older mothers whereas Fe increased with increasing maternal age but decreased for heavier babies. Copper, Fe and Zn in human colostrum milk from 50 Brazilian mothers were measured using TXRF with SR in a study reported by da Costa *et al.*[60] Mean concentrations found were 0.54 ± 0.29 mg l^{-1} Cu, 1.72 ± 1.01 mg l^{-1} Fe and 6.97 ± 2.82 mg l^{-1} Zn, which were comparable to other values in the literature. Zarkadas *et al.*[61] showed that U could be determined in urine by TXRF. Chemical treatment and preconcentration were necessary but the method was only suitable for measuring concentrations of U above normal.

Selenium depletion was found in 2-month old suckling calves using TXRF measurement of Se in serum. In this study, reported by Buoso *et al.*,[62] Se concentrations in the serum of 78 calves ranged from 10 to 66 μg l^{-1}, lower than the expected range (60–80 μg l^{-1}). The results corroborated a clinical diagnosis of Se deficiency.

For a study of *trace elements in liver disease*, Loguercio *et al.*[63] measured Br, Fe, Se and Zn in plasma and erythrocytes by PIXE. Liver cirrhosis resulted in a significant decrease in Fe, Se and Zn in plasma and Se in erythrocytes when compared with a control group. This decrease was not related to the degree of impairment of liver function and was only partially affected by nutritional status. Plasma Br was higher in cirrhotics than in healthy controls.

1.3.3.5 Determination of elements in tissues by XRF. Concentrations of 14 elements in *liver, brain and kidney* of patients with liver cirrhosis were measured by Carvalho and Marques[64] using XRF. Results for As, Ni and Sr were low, near the LOD of the technique. Concentrations of Co, Fe and Pb were higher and Se and Zn lower than in the corresponding tissues from subjects free of liver disease. However, in kidney the Zn concentration was higher in cirrhotic patients. In a study of liver Zn in Greenlandic Inuit measured by XRF, Laursen *et al.*[65] found no significant difference in concentration from that found in Danes. For neither group was there a significant difference between results for males and females. However, there was a significant positive correlation between liver Zn and age in Danish women but not in Inuit or in Danish men.

In the development of an XRF method suitable for determining *copper, iron and zinc in skin*, Bagshaw and Farquharson[66] prepared skin phantoms which were analysed with fluorescence from a Ge secondary target irradiated with a high output tungsten target X-ray tube. Calibration models were constructed to allow quantitation, with spectral analysis performed using the Marquardt method of non-linear least squares fitting. The LODs were around 5 μg g^{-1} for Cu and Zn and around 10 μg g^{-1} for Fe, which are comparable to levels encountered in healthy skin.

Platinum from cisplatin has been determined in human cancerous tissue obtained by biopsy in a study reported by Suzuki *et al.*[67] With monochromatic Mo K alpha radiation as a source and a LiF crystal, an LOD of 0.01 μg g^{-1} was achieved. The technique was used to study samples taken from patients with advanced bladder cancer.

In an attempt to find *magnetic materials in birds and fish* that could possibly interact with the earth's magnetic field and enable them to sense direction and location, Harada *et al.*[68] looked for Fe in otoliths of sea fish and birds with SRXRF. In the saccular and utricular otoliths, detectable levels of Fe were rarely found, but in the lagenal otoliths of birds, significant quantities of Fe were found. They suggested that the lagenal otoliths contain tiny magnetic particles of low inertia that are displaced by applied magnetic fields, providing the bird with geomagnetic sensory input from which the brain could infer navigational information.

Stocklassa *et al.*[69] evaluated the commercial ITRAX X-ray spectrometer for *the analysis of human hair samples*. It was capable of measuring element concentrations down to 1 μg g^{-1} and was used to construct a database of normal values for physiologically important elements in healthy Swedish subjects.

1.3.4 Other multi-element techniques and studies. Correia *et al.*[70] developed a method to determine Mn and Se in serum by *simultaneous ETAAS*. Samples were diluted 1 + 3 with 1% v/v HNO_3–0.1% w/v Triton X-100. A Pd–$Mg(NO_3)_2$ modifier was added and a heating program with pyrolysis at 1200 °C and atomisation at 2300 °C was applied. Buildup of carbonaceous residues on the integrated platform was a problem which was overcome by addition of an oxidizing mixture (15% w/w H_2O_2–1% v/v HNO_3) and an additional low temperature pyrolysis step at 400 °C. The method showed satisfactory results with a Seronorm serum RM and good recoveries of Mn and Se added to five serum samples. In a further method to determine Cu, Fe and Zn simultaneously by ETAAS,[71] the higher sensitivity for Zn was a problem. They solved this by selecting a pyrolysis temperature (700 °C) above the normal maximum temperature. The losses of Zn brought the sensitivity down to a level comparable to Cu and Fe. Samples were diluted 1 + 79 with 1% v/v HNO_3–0.01% w/v Triton X-100 and, to keep the sensitivity

within the linear range, the sample volume injected was reduced to 5 µl and a gas flow of 50 ml min^{-1} was introduced during atomisation. The method was validated by analysis of a Seronorm serum RM and by recovery experiments.

Non-dispersive atomic fluorescence spectrometry with two channels allowed Lu *et al.*[72] to develop a sensitive method to determine Cd and As simultaneously in biological samples. Volatile species were generated by reduction with $NaBH_4$ and, under optimised conditions, LODs of 10 ng Cd l^{-1} and 150 ng As l^{-1} were attained.

A method to sequentially determine selenium and tin in human brain tissue was developed by Szoboszlai *et al.*[73] Samples were dissolved by microwave digestion and the elements determined by ETAAS with Zeeman background correction and the transversely-heated graphite atomizer. For Se determination a prereduced Pd modifier was found best, whereas for Sn a Pd–$Mg(NO_3)_2$ modifier was preferred. Accuracy was demonstrated by analysis of CRMs and by recovery experiments. In autopsy samples from subjects with no diseases of the central nervous system, Se concentrations ranged from 200–700 ng g^{-1} and Sn from 20–300 ng g^{-1}.

There have been two interesting papers by Hol *et al.* exploring *the relationship between selenium and mercury from dental amalgam*. Selenium is believed to have a protective effect in detoxifying Hg. Their study on urinary excretion[74] showed that a group of subjects with amalgam fillings excreted less Se (median 36.4 µg) in urine over 24 h than a control group without amalgam (median 47.5 µg). Measurements were by HGAAS. There was, however, no significant difference in Se excretion between groups with and without amalgam-related symptoms. In their study on whole blood Se,[75] however, they found that the median blood Se (119.2 µg l^{-1}) of the group with symptoms was lower than those with amalgam fillings but without symptoms (130.3 µg l^{-1}). The latter group showed no significant difference from those in a control group without amalgam fillings.

Studies by Burguera and co-workers have given data on *element concentrations in teeth and bones*. Reference values for elements in deciduous teeth of Venezuelan children were reported.[76] They collected 67 teeth from children of mean age 7.3 y, powdered the teeth and analysed the samples for Ca, Mg, Sr and Zn by FAAS and Cu and Pb by ETAAS. There were no significant differences in composition with age and sex and only for Sr was there a significant difference between different tooth types. However, it should be noted that Rahman *et al.*[77] collected tooth samples from children at 9 primary schools in the Karachi region and showed that incisors had significantly higher levels of Pb than either molars or canine teeth, an observation that is consistent with most previous studies. Positive correlations were found for Sr—Cu, Sr–Pb and Sr–Zn and negative correlations for Ca–Pb and Ca–Zn. A wide range of Ca and Sr concentrations in human bones was found in a further study.[78] Bone samples taken from patients having repairs to bone fractures were digested and the Ca and Sr determined by FAAS with a N_2O–C_2H_2 flame. The ranges found were 100–650 mg Ca g^{-1} (mean: 253 mg g^{-1}) and 16–81 µg Sr g^{-1} (mean: 33 µg g^{-1}). There was a significant decrease in both elements concentrations after age 55 y for males and after 45 y for females.

In a study of *nutrition* in trauma patients during continuous renal replacement therapy, Klein *et al.*[79] found significant loss of Ca and Mg which was not compensated for by the amount present in standard parenteral nutrition formulae. They measured Ca, Mg, N and Zn in urine, effluent and dialysate to assess output and calculated input from intake records. The metals were determined by AAS and urea N by conductivity changes after addition of urease. Urea N was removed in amounts similar to those in normal kidney function and the Zn supply was adequate. In a study of Se and Zn nutrition in 103 elderly New Zealand women, de Jong *et al.*[80] found that mean plasma Se (0.85 ± 0.23 µmol l^{-1}) and Zn (12.4 ± 1.4 µmol l^{-1}) were evidence of suboptimal status. Estimated dietary intakes were 34 ± 10 µg Se and 8.7 ± 2.0 mg Zn.

A technique for studying *the binding of metals to proteins in blood fractions* was developed by Pomazal *et al.*[81] They combined hydrophobic interaction chromatography to separate the proteins in plasma and in lysed erythrocytes with off-line ETAAS measurement to determine Co, Cr, Cu, Fe, Mn, Ni and Zn in 4 ml fractions. The metal profiles obtained were compared with the protein chromatograms.

In an attempt to understand *how metal ions released from nickel-based alloys are accumulated in cells*, Messer and Lucas[82] exposed human gingival fibroblasts *in vitro* to Be^{2+}, Cr^{6+}, Cr^{3+}, Ni^{2+} and Mo^{6+} for 72 h and measured these elements by AAS in cell fractions. The Cr^{3+} concentrated in the low-density molecule fractions and plasma membrane fractions which, they concluded, corresponded to its inability to readily cross membranes. The highest Cr^{6+} concentrations were found in the plasma membrane and nuclear fractions followed by the mitochondria fraction. This, they indicated, corresponded to oxidation by Cr^{6+}, giving Cr^{3+} which accumulated at the membrane. Penetration of Cr^{3+} unchanged into the nucleus altered nuclear and mitochondrial function. The Ni^{2+} concentrated in the cytosol fraction.

Concentrations of seven *trace elements in the cervical mucus* of 45 healthy Taiwanese women were reported by Chuang *et al.*[83] Measurements of Cd, Cr, Cu, Fe, Ni, Se and Zn were made by ETAAS. A significant positive correlation was found between age and Se concentration. Significant differences were found for Ni between four different age groups, but none for the other elements.

1.4 Developments in single element techniques

Ji and Ren[84] developed *the microsampling technique in FAAS* further by taking the derivative of the signal. For Cu and Zn in 100 µl volumes, the LODs at 13 and 8 µg l^{-1}, respectively, were 4.5- and 6.5-fold better than with conventional peak measurement. The method was applied to the determination of Cu and Zn in the serum of rats. Accuracy was shown by good recovery of standard additions and by analysis of a digest of a Porcine Liver CRM.

A direct flame solid sampling technique for analysis of powdered biological samples by FAAS was developed by Flores *et al.*[85] A weighed amount was transferred to a small polyethylene vial in a glass chamber. A flow of air through the chamber carried the powder as an aerosol into a flame-heated T-cell in the optical path. The integrated signal was proportional to the amount of the element in the sample. This approach was applied to the determination of Cu in bovine liver samples which were ground to a particle size less than 80 µm diameter. Results compared well with those obtained after sample digestion and conventional FAAS.

The *tungsten-coil atomizer* was used by Silva *et al.*[86] to determine Dy and Eu in digests of sheep faeces. These elements were used as markers to determine the passage rate of feed through the animal's digestive tract. Samples were digested in HNO_3–$HClO_4$ and the results were compared with those obtained by ETAAS with a graphite furnace. Results for Dy were not good in the graphite furnace because of memory effects from carbide formation: Eu was not affected in this way. The LODs in the tungsten-coil atomiser (6.9 µg l^{-1} for Dy and 2.1 µg l^{-1} for Eu) compared with figures of 2.2 µg l^{-1} and 5.2 µg l^{-1}, respectively, for the graphite furnace. The lifetime of the W-coil (200 firings) was 3-fold higher than for a graphite tube in these determinations. A permanent modifier of Rh was investigated by Zhou *et al.*[87] for its suitability for the determination of Pb in blood and urine by tungsten-coil ETAAS. They found that the Rh not only effectively stabilised Pb in the pyrolysis step but also helped the removal of

carbonaceous residues in the cleaning stage. Thus the power in the final stage could be reduced, which extended the lifetime of the filament to over 300 firings. Direct calibration with aqueous standards was possible and accuracy was verified by the analysis of CRMs.

A permanent modifier of iridium was found by Grinberg *et al.*[88] to be suitable for the determination of Cd and Pb in digests of tissue by FAPES. Matrix interference was compensated for by standard additions calibration.

High sensitivity in the determination of chromium in serum was achieved by Ezer *et al.*[89] using ETA-LEAFS. A tunable dye laser coupled to a frequency doubling crystal produced radiation at 236.5 nm to excite Cr to fluoresce at 302.2 nm and 357.9 nm. An LOD of 4 ng l^{-1} obtained in water using a 20 µl sample injection was limited by the blank signals from traces of Cr in the graphite material. The technique was applied to the determination of Cr in gastrointestinal perfusate and serum samples in a study of rats subjected to heat stress; samples were diluted 1 + 1 and 1 + 49 with deionised water, respectively.

Camero *et al.*[90] described *the use of tungsten probes to introduce samples* into a graphite furnace in a method for the determination of Cu in human seminal plasma. The probe loaded with a volume of the undigested sample was introduced into the graphite tube and heated by radiant heat to dry and pyrolyse the sample and then atomise the Cu. The LOD (4.8 µg) was better than that obtained with acid-digested samples introduced with an autosampler (11.2 µg) but reproducibility was not as good because of the heterogeneous distribution of Cu in the matrix. Ultrasonic stirring prior to analysis improved the precision.

A new approach to immunoassay is to use atomic spectrometry to measure the metal in metal chelate-labelled antibodies. The use of metal-labelled antibodies is now common but detection is normally by time-resolved molecular fluorescence spectrometry. Zhang *et al.*[91] used ICP-MS to measure Eu in the determination of thyroid-stimulating hormone (TSH). The TSH was captured by anti-TSH monoclonal antibodies, immobilised on a solid support. Labelling agents containing Eu were then added and unbound reactants washed away. The Eu was extracted with 1% v/v HNO_3. The precision within- and between-batch was better than 10% RSD and results correlated well with those obtained by radioimmunoassay. In their method for alpha-fetoprotein (AFP) in serum, Wang *et al.*[92] used a Cd-chelate as a label and determined Cd by ETAAS. Results compared well with those found by time-resolved fluoroimmunoassay. Inductively-coupled plasma MS allows the determination of more than one element at the same time. Quinn *et al.*[93] have therefore investigated the possibility of measuring more than one analyte by immunoassay by using tagging with different elements. They showed that they were able to determine two proteins at the same time in this way.

1.5 Reference materials

Parsons *et al.*[94] described the preparation and validation of *four reference materials for lead in blood and four for lead in urine*. These were circulated to 21 selected laboratories to obtain certified values. These laboratories used ETAAS, ASV and ICP-MS to determine Pb. The certification of the blood samples was satisfactory but the analysis of the urine RMs gave more problems, particularly at concentrations above 600 µg l^{-1}.

1.6 Hair and nail analysis

Washing procedures for removing externally-bound elements on hair were examined by Morton *et al.*[95] In experiments with simulated sweat spiked with toxic elements, they found that the elements As, Hg, Sb and Se were irreversibly bound and were not removed by any of the washing procedures examined. However, Cd, Cr and Pb were removed by washing with 0.1 M HCl. The hair samples were digested with HNO_3–H_2O_2 and the elements determined by ICP-MS. In a separate study[96] they showed that it was not possible to differentiate between exogenously-bound and endogenous inorganic Hg and methylmercury. Maurice *et al.*[97] showed that exogenously applied Tl was removed by soaking in water for 24 h or by using the IAEA recommended method using successive washes in water, acetone and water. These procedures led to no significant difference in results on a hair sample from a Tl-poisoned patient in which the Tl was tightly bound in the hair structure.

A micro-scale *digestion procedure* for determination of As in hair was developed by Flores *et al.*[98] The procedure of washing, reagents addition, digestion and completion to volume were carried out in small disposable polypropylene vials. Digestion was with H_2SO_4–HNO_3 with microwave heating and then determination by HG-AAS. However, recovery was not 100%, but the addition of HCl at a specific stage in the heating programme improved recovery and gave satisfactory results. Kamogawa *et al.*[99] preferred direct analysis using slurry atomisation. Samples were pulverised by cryogenic grinding for 13 min and slurried in 0.1% v/v CFA-C, a mixture of tertiary amines. The elements Cd, Cu and Pb were determined by ETAAS.

The longitudinal distribution of *thallium in hair* was studied by Maurice *et al.*[97] using ICP-MS with ID and ETV. Of the several methods they tried for handling small hair samples, the most successful was to glue three strands together with pressure-hardening glue (superglue). This was then cut into 10 mm segments and inserted with a solid sample injector into the furnace. Measurements on the hair of a Tl-poisoned patient gave a concentration of 0.4 µg g^{-1} at the root, which fell to 0.01 µg g^{-1} at the end of the hair.

Saad and Hassanien[100] used HG-AAS in their study of *arsenic concentrations in the hair* of Egyptians not occupationally exposed to As. The concentrations ranged from 0.04 to 1.04 µg g^{-1} with 43% above a quoted reference range (<0.25 µg g^{-1}). Concentrations in children and adolescents (mean 0.35 µg g^{-1}) were significantly higher than adults (mean 0.23 µg g^{-1}). Principal sources of exposure were found to be smoking, and fish and animal protein in the diet.

Morton *et al.*[96] achieved a straightforward procedure for speciation of *mercury in hair* after cold digestion overnight with HNO_3–H_2O_2. The digest was separated by HPLC on a C_{18} reversed-phase column with 5% CH_3OH–0.1% 2-mercaptoethanol–0.06 M ammonium acetate and the species detected by ICP-MS. They reported that Hg was lost when microwave pressure digestion with HNO_3–H_2O_2 was used. In their method, Chen *et al.*[101] used ETAAS for measurement. For total Hg, the sample was digested with HNO_3, the Hg complexed with 2,3-dimercaptopropane-1-sulfonate at pH 5–6 and preconcentrated onto SepPak C_{18} cartridges. This method would measure down to 0.06 µg g^{-1}. Methylmercury was determined by extracting first with 2 M HCl for 1 h with ultrasonic assistance and then measuring Hg in the supernatant. The remaining hair residue was used to measure inorganic mercury. The sum of the measured methylmercury and inorganic Hg was close to the measured total Hg. Dietz and Bayona[102] determined methylmercury in hair by GC with CVAFS detection after acid-digestion, aqueous ethylation and headspace solid-phase microextraction sampling. The LOD was 50 ng g^{-1} for 100 mg of hair. The mean methylmercury concentration in an urban Spanish population was 0.76 ± 0.73 µg g^{-1}. Mercury in the hair of gold mining communities in the Philippines was measured by Murao *et al.*[103] using a standardless PIXE method. Amalgamation and smelting are usually done inside houses, especially in the kitchen. Hair levels of mercury in the women were higher than in the men as the women often did the processing and stayed longer in the house.

Concentrations of 19 elements in the mane hair of 24 *thoroughbred racing horses* were determined by ICP-AES in a study reported by Assano *et al.*[104] No significant differences were found between male and female. There were significant positive correlations with age for Cd and Mo and negative correlations for Fe, Hg and Mn.

1.7 Drugs and pharmaceuticals

Interest in determining *the toxic and essential trace elements in Chinese medicinal materials* continues. Chen *et al.*[105] described a simple, rapid method for the determination of Hg using a pyrolysis unit coupled to an AA spectrometer. Direct analysis of 20 mg samples down to 66 pg Hg was possible. The results compared well with those obtained by CVAAS and ICP-MS after digestion. The same group has used moveable reduction bed hydride generation with ICP-MS to simultaneously determine As, Ge, Hg and Se in medicinal materials.[106] Ultrasonic slurry sampling was developed by Amin *et al.*[107] to introduce herbal medicinal samples into a molybdenum-tube atomiser for the determination of Mn by ETAAS. The slurry medium, 10% glycerol, also acted as a modifier in removing matrix interference. Comparison of results with those obtained after acid digestion showed good agreement. Data obtained by Dong and Zhu[108] on the Suxiao Jiuxin pill by FAAS showed that it was rich in Ca, Cu, Fe, Mg and Zn, which may have had a beneficial effect in its use in treating coronary heart disease.

Hem[109] studied *the absorption and elimination of aluminium-containing adjuvants in pharmaceuticals. In vitro* studies had shown that citric acid, lactic acid and malic acid in interstitial fluid are capable of dissolving Al from the adjuvants, amorphous $AlPO_4$ and crystalline $Al(OH)_3$, with more rapid dissolution from $AlPO_4$. Experiments on rabbits with ^{26}Al-labelled adjuvants administered intramuscularly followed by measurements with AMS showed that ^{26}Al was present in the blood after 1 h. The integrated blood Al response over 28 d revealed 3-fold more absorption from $AlPO_4$ than from $Al(OH)_3$.

1.8 Marine and freshwater biology

This section should cover measurements on marine and freshwater organisms relevant to environmental effects. These also affect the quality of seafood and freshwater fish and it is often difficult to distinguish what relates to this section and what is the province of the foods section. Thus, the very important subject of accumulation of Hg in fish, which is pertinent to human dietary intake of Hg, is dealt with in section 2.9.5.

Using XRF, Carvalho *et al.*[110] measured 15 *elements in the tissues* of 15 *Delphinus delphis* and two *Tursiops truncatus* dolphins from the Portuguese coast of the Atlantic Ocean. Lyophilised samples of muscle, liver, fat tissue and skin were pressed into pellets for measurement. Highest concentrations of Cu, Hg and Mn were found in the liver with Se and Zn highest in the skin. Concentrations of Co, Ni, Pb, Rb and Sr were low and showed relatively little difference between tissues. Concentrations of heavy metals in four fish species from three different sites on the Saudi Arabian coast of the Arabian Gulf were measured by Al-Saleh and Shinwari[111] using AAS. Mean concentrations of As, Cd, Ni, Pb and V were 42.7, 4.6, 60.6, 20.0 and 73.6 ng g wet weight^{-1}, respectively, and were below limits for human consumption.

A comparison of *extraction procedures for the determination of As and other elements* in lobster tissue by Brisbin and Caruso[112] revealed that microwave-assisted extraction at 75 °C for 2 min was generally the best. It was the mildest, fastest, least complicated and most reproducible. It gave comparable or improved recoveries for all of the analytes measured. However, Kirby and Maher[113] found that microwave-assisted extraction did not always give complete recovery. They used three extractions with 1 : 1 CH_3OH–H_2O at 70–75 °C for 5 min when analysing freeze-dried marine animal tissue with determination by HPLC-ICP-MS. Whereas quantitative extraction of water-soluble As species for dogfish muscle (DORM-2 CRM) was attained, efficiency was lower for liver, digestive tract and some whole tissue (*e.g.* mussel).

The subject of *arsenic speciation* seems to get more complex each year. Geiszinger *et al.*[114] have identified another As-containing betaine, trimethylarsoniopropionate, in muscle, liver, kidney and lung tissue of a sperm whale, *Physeter catodon*, that was beached on an island in the Andaman Sea. Aqueous extracts of the tissues were separated by HPLC and the As detected by ICP-MS. Arsenobetaine was the dominant As species in all tissues.

1.9 Progress for individual elements

1.9.1 Aluminium. A *permanent Ru chemical modifier* was used by Magalhaes *et al.*[115] for the determination of Al in human serum and urine using ETAAS. The authors established that the optimum pyrolysis and atomisation temperatures were 1300 °C and 2300 °C for serum, and 1000 °C and 2400 °C for urine with a graphite tube coated with 500 μg of ruthenium. Calibration was performed with aqueous standards and the reported LOD was 0.4 μg l^{-1} for both sample matrices. Atomisation signals were observed to be symmetrical and background signals were very low. The tube lifetime was reported to be over 600 firings.

Sanz-Medel *et al.*[116] presented *a very comprehensive review of analytical procedures for the chemical speciation of Al in human serum.* The group examined in detail experimental and instrumental conditions for identification of high M_r (HM_r) and low M_r (LM_r) Al species. Non-chromatographic separation methods coupled with ETAAS were compared with chromatographic methods (size exclusion, anion exchange and fast protein liquid chromatography) coupled with either ETAAS or ICP-MS. The reviewers identified that most of the serum Al was bound to transferrin, whilst Al in the LM_r fraction, which represented some 10–20% of total serum Al, was associated with citrate or phosphate and as an Al–citrate–phosphate complex. Halling *et al.*[117] reported the findings of a large study of Al concentrations in deciduous teeth. The researchers determined Al concentrations in 323 deciduous teeth from Swedish children using ETAAS. The Al concentration varied significantly with tooth type. The mean Al concentration in incisors was 1.05 ppm compared with 0.48 ppm in canines and 0.53 ppm in molars. A significant difference was also observed between teeth with and without caries.

A study of Al exposure in potroom workers from a newly constructed primary Al smelter was undertaken by Rollin *et al.*[118] Blood and urine Al concentrations were determined in a group of 115 newly employed workers with no previous exposure to Al, using AAS. The authors also used AAS to determine ambient air Al levels in the potroom. The authors noted an early increase in blood Al levels following exposure to very low air levels of Al in the workplace, and that after 12 months blood Al levels reached a plateau. In contrast, urine Al levels continued to rise over a 36 month monitoring period, reaching a mean value of 49 μg l^{-1}, which suggested a slow elimination rate. Drueke[119] presented a review summarising *studies on Al absorption* using the very sensitive AMS technique. The author reported that current estimates of intestinal absorption of Al were in the range 0.06–0.1% and that absorption was influenced by systemic and local factors, particularly those with which Al complexed in the gut. It was argued that lessons learned from the Al studies would provide valuable guidance in the safety evaluation of other potential toxic elements used as therapeutic agents for patients with renal failure. Yokel and colleagues[36] used AMS to determine the entry, half-life and elimination of ^{26}Al from the brains of rats

administered a single intravenous infusion of ^{26}Al. The Al was administered either as an Al–transferrin species or as Al–citrate, the major low MW species. The peak brain Al concentration was 0.005% of the dose irrespective of the Al species given. The half-life of elimination of Al from the brain was determined to be 150 d. Administration of the Al chelator desferrioxamine reduced the elimination half-life of brain Al to 53 d. The authors concluded that a small fraction of blood Al enters the brain and persists for a considerable time.

Reusche *et al.*[120] reported the tragic case of a *fatal Al encephalopathy* after reconstructive neurosurgery. Bone reconstruction was performed on a patient, following surgery on the inner ear, using an Al containing bone cement. A short period afterwards the patient exhibited symptoms similar to dialysis encephalopathy and died six months later. Levels of Al determined at autopsy in the brain cortex and subcortex by AAS were up to 9.3 μg g^{-1} compared with a 'normal' brain Al concentration of <2 μg g^{-1}. Microscopic examination of CNS tissue showed changes characteristic of dialysis associated encephalopathy. The authors highlighted the extreme neurotoxicity of Al, which in this case was caused by about 30 mg of Al, a fraction of which appeared to have direct access to the brain *via* the cerebrospinal fluid. Finally, Hern *et al.*[109] used AMS to determine ^{26}Al in blood samples from rabbits administered $AlPO_4$ and $Al(OH)_3$ adjuvants. The group also examined *in vitro* dissolution of Al adjuvants by hydroxycarboxylic acids in interstitial fluid. They concluded that Al containing adjuvants administered intramuscularly are dissolved by interstitial hydroxycarboxylic acids, such as citrate, absorbed into the blood and distributed to body tissues.

1.9.2 Antimony. A method for the *sequential determination of Sb^{III} and Sb^{V} in biological matrices using FI-HG-AAS* was described by de Pena *et al.*[121] The Sb^{III} and Sb^{V} ions were sequentially extracted 'on-line' from solid lyophilised blood or liver tissue with 1.5 M CH_3COOH and 0.5 M H_2SO_4, respectively. The released Sb^{V} was subsequently reduced to Sb^{III} by on-line reaction with L-cysteine. Reported LODs were 1.0 μg l^{-1} for Sb^{III} and 0.5 μg l^{-1} for Sb^{V} and recoveries between 97% and 103% were obtained from bovine liver samples spiked with both Sb species.

Miekeley *et al.*[122] used ICP-MS coupled with on-line ion chromatography to monitor *Sb species in blood, urine and hair of leshmaniasis patients* treated with *N*-methylmeglumine antimonate. Total Sb concentrations of up to 250 μg l^{-1} and 60 mg g^{-1} creatinine were reported in blood and urine, respectively, following 30 consecutive injections of 5 mg Sb per kg body weight. Antimony concentrations of up to 24 μg g^{-1} were determined in the hair of these patients. The parent drug was separated from inorganic Sb^{III} and Sb^{V} species by on-line ion chromatography using an anion exchange column and 2 M or 20 M EDTA, pH 7.4 as the mobile phase. The reported LOD for both ion species was 1.6 μg l^{-1}.

1.9.3 Arsenic. Methods continue to be described for the *accurate determination of low levels of As in biological matrices* to monitor both environmental and occupational exposures to the element. Lu *et al.*[72] described a very sensitive method for the simultaneous determination of As and Cd in biological matrices by HG-AFS. The authors investigated the optimum conditions for the generation of volatile hydrides of both As and Cd using KBH_4. The elements were quantitatively determined using a double channel atomic fluorescence spectrometer with an intermittent flow reactor. Reported LODs were 150 ng l^{-1} and 10 ng l^{-1} for As and Cd, respectively. The method was used to determine both elements in a range of biological specimens. Flores *et al.*[98,123] undertook studies to reduce the interference of volatile nitrogen oxide species, generated by HNO_3 digestion of hair samples, on the determination of As in hair using HG-AAS. The researchers examined six different digestion procedures and ranked their performance based on the recovery of inorganic and organic As species from spiked samples and on agreement with the certified value for a hair CRM. The preferred method involved microwave digestion with H_2SO_4, HNO_3 and HCl added at specific stages in the microwave programme. The digested samples were mixed with sulfamic acid, diluted with H_2O and L-cysteine was added as a pre-reductant for As determination by HG-AAS. The authors noted that, with addition of sulfamic acid, results obtained for the hair CRM were in good agreement with the certified value, but if it was omitted, results were low and high background signals were observed. Urea, benzoic acid and hydroxylamine hydrochloride were all less effective than sulfamic acid in overcoming interferences on the As signal. Wu *et al.*[124] determined As in human whole blood using HG-AAS in a study to investigate the relationship between blood As and antioxidant capacity in Taiwanese subjects exposed to contaminated water. A chemiluminescence method was used to measure plasma concentrations of superoxide as a marker of reactive oxidants. The authors reported a range of blood As levels from 0 to 46.5 μg l^{-1}, with a mean value of 9.6 μg l^{-1}. They observed that blood As showed a positive correlation with the plasma reactive oxidant level and an inverse relationship with plasma antioxidant capacity. They hypothesised that ingestion of As contaminated water might cause a persistent oxidative stress in peripheral blood, which may be a contributory mechanism underlying the carcinogenesis and atherosclerosis associated with chronic As exposure.

Hinwood and colleagues[3] investigated *whether 24 h urine collections or creatinine correction were necessary* for the determination of urinary As in population studies of environmental As exposure. Spot urine samples and corresponding 24 h urine collections were obtained from 160 volunteers and urine As determined by HG-AAS. The authors reported a significant correlation between adjusted and non-adjusted urine As levels and concluded that creatinine adjustment may not be required for population studies on environmental As exposure.

Apostoli *et al.*[125] examined the effect of inorganic As and organometallic As species; monomethylarsonate (MMA), dimethylarsinic acid (DMA) and arsenobetaine (AB) on the *excretion of porphyrin homologues* in a group of art glass workers. Total urine porphyrins were determined by HPLC and urinary As species determined using HPLC-ICP-MS. A significantly increased excretion of penta- and uroporphyrins was observed which the authors hypothesised was due to the As inhibition of uroporphyrin decarboxylase in the haem synthesis pathway. They concluded that determination of urine porphyrins may be useful to assess early effects of As exposure on a group and individual basis.

Sternowsky *et al.*[126] used HG-AAS to determine *As concentrations in breast milk* of nursing mothers living in a potentially As contaminated region of lower Saxony and in two uncontaminated regions. The As concentration was below 0.3 μg l^{-1} in more than 80% of the collected samples. The highest measured As value was 2.8 μg l^{-1} determined in a sample collected from a rural area. The mean As concentration was similar in all three regions and the calculated daily intake for breastfeeding infants was between 0.02–0.06 μg kg^{-1}, which was far below the WHO limit of daily permissible intake for adults.

Several groups have reported the results of studies *on As speciation in biological matrices*. Kirby and Maher[113] described a method for the quantitative extraction of water soluble As species from freeze dried marine biological tissues for determination by HPLC-ICP-MS. Optimum conditions for microwave assisted extraction were triplicate extraction with 50% CH_3OH–H_2O v/v at 70–75 °C for 5 min. Using these conditions, extraction of As from the biological CRM DORM-2 was around 100%. However lower extraction

efficiencies, between 66% and 92%, were reported for liver, digestive tissue and whole mussel tissue. The authors concluded that efficiency of extraction of As was strongly dependent on marine animal species and tissue type. Csanaky and Gregus[127] compared the urinary and biliary excretion of As in five animal species. Rats, mice, hamsters, rabbits and guinea pigs were injected with either As^{III} or As^{V}, bile and urine samples were collected and As species separated and quantitatively determined using HPLC-HG-AAS. The researchers observed that all animal species injected with As^{V} excreted more As in urine than bile whereas, with the exception of rabbits, injection of As^{III} led to more excretion in bile than urine. Arsenic species determined in bile were almost exclusively trivalent (As^{III} or MMA^{III}) while both trivalent and pentavalent species (As^{V}, DMA^{V}, MMA^{V} and As^{III}) were determined in urine. All animal species with the exception of guinea pigs produced the toxic MMA^{III} metabolite, which was excreted in bile. Gong *et al.*[128] investigated the oxidation stability of the recently identified As metabolites MMA^{III} and DMA^{III} in water and human urine. Samples of H_2O and urine containing the two trivalent As species were stored for up to 5 months at 25 °C, 4 °C or −20 °C. The As species were quantitatively determined by HPLC-HG-AFS, which offered LODs down to sub μg l^{-1} levels for each As species. The authors found that oxidation of both MMA^{III} and DMA^{III} was matrix and temperature dependent. In urine, the MMA^{III} species was completely oxidised within a week at 25 °C and most (90%) was oxidised over the 5 month period at both 4 °C and −20 °C. The DMA^{III} species was even less stable with complete oxidation to DMA^{V} within a day at 4 °C and −20 °C. The authors concluded that both these newly identified metabolites are much less stable than other As species.

1.9.4 Bismuth. Burguera *et al.*[129] described a *method for the determination of Bi in a wide range of biological tissues using ETAAS*. Samples of approximately 100 mg were microwave digested with HNO_3–H_2O_2. Platinum and tartaric acid were added to the digested samples as chemical modifiers. The addition of 4% w/v tartaric acid was observed to improve the stabilising effect of the Pt. An LOD of 0.1 μg g^{-1} and characteristic mass of 22 pg were reported. The method was validated by determination of Bi in whole blood and urine RMs.

1.9.5 Boron. There continues to be interest in the quantitative determination of B in biological matrices. Burguera *et al.*[130] undertook a *comprehensive comparative study of potential chemical modifiers for the quantitative determination of B in blood, urine and bone by ETAAS*. The group examined the efficacy of commonly used chemical modifiers in combination with coating treatment of a pyrolytically coated graphite tube using a longitudinally heated electrothermal atomiser. They observed that many modifiers used with a tungsten–rhodium coating led to erratic and noisy signals, whilst Ni and Pd modifiers and a tungsten-coated tube had too high background absorption signals for determination of B. Optimum performance was found with a zircon–citric acid chemical modifier and a zircon-coated tube. The zircon coating improved the thermal stability of B, allowing high pyrolysis temperatures without analyte loss, whilst the addition of citric acid improved the m_0 for B to 282 pg. The reported LOD was 60 μg l^{-1}. This was reported to be sufficiently sensitive for the determination of B in urine and bone but still not sensitive enough for the determination of B in the blood of healthy subjects. The authors used the method to determine levels of B in blood, urine and femur bone samples from patients with osteoporosis. The measured values were in good agreement with previously reported values.

During *boron neutron capture therapy* (BNCT) for cancer, the intensity and timing of irradiations is determined by monitoring ^{10}B concentrations in blood. Laakso *et al.*[15] described a method for the determination of B in the blood of patients undergoing BNCT using ICP-AES. Whole blood or blood plasma samples were treated with TCA for deproteinisation before solution nebulisation, to determine the B concentration. Recoveries of B in spiked whole blood were between 95.6 and 96.2%. Erythrocyte B levels were estimated indirectly from the whole blood and plasma B levels and the blood haematocrit. The method was compared with an established ICP-MS method, which used a wet digestion procedure for sample pre-treatment. A good correlation (r = 0.994) between the two methods was observed. The authors considered the method to be one of the fastest for quantitative determination of B during BNCT.

1.9.6 Cadmium. There appears to be a renewed interest in a number of elements during this review period, including Cd. Grinberg *et al.*[88] selected *Ir as a permanent chemical modifier* for the determination of Cd and Pb in biological tissues by FAPES. The authors described the tube coating procedure and furnace temperature programme for optimum sensitivity and minimal background signal. Results for the analyses of CRMs using standard additions calibration gave good agreement with certified values and LODs of 2.2 ng g^{-1} and 4.1 ng g^{-1} were reported for Cd and Pb, respectively, in DOLT-2 and TORT-2 RMs.

Several groups have reported *levels of Cd in human body fluids and in healthy and diseased tissue*. Panayi and colleagues[131] determined levels of Cd and Zn in brain tissue from subjects diagnosed with Alzheimer's disease, patients with senile involutive cortical changes and healthy subjects using ICP-MS. The researchers determined concentrations of both elements in 6 brain regions. For Cd, they found no significant differences in Cd levels between normal and diseased tissues for all brain regions examined. In contrast, they found that Zn levels were significantly decreased in Alzheimer's subjects in all regions.

Paoliello *et al.*[132] investigated the exposure to Cd and Pb of children living in a mining region of Brazil. Blood samples, taken from children living in both urban and rural areas around the mine and associated refinery, were analysed for Cd and Pb using ETAAS with Zeeman-effect background correction. Levels of Cd in blood for most of the subjects were below the LOQ of 0.5 μg dl^{-1}. Median blood Pb levels were 11.25 μg dl^{-1} in children living close to the mine and 4.4 μg dl^{-1} in children from more distant rural communities. Satarug and colleagues[133] determined levels of Cd in urine and tissues of Australians with no history of occupational metal exposure. Tissue and urine Cd was quantitatively determined using ICP-MS. Mean Cd levels in lung, liver and kidney were reported to be 0.13 μg g^{-1}, 0.95 μg g^{-1} and 15.45 μg g^{-1}, respectively. The authors observed that renal Cd levels were higher in females than in males of a similar age and with a similar lung Cd burden, which they hypothesised was due to a higher renal Cd absorption rate. Nishijo *et al.*[134] reported the findings of an interesting study on the effects of *maternal Cd exposure on pregnancy outcome and on Cd in breast milk*. The author used AAS to determine Cd in urine and colostrum milk from 57 mothers. They observed that the rate of preterm deliveries was higher in mothers with urine Cd levels greater or equal to 2 nmol $mmol^{-1}$ creatinine. Similarly, birth weight and height were significantly lower in infants of mothers with higher urine Cd concentrations. The authors also noted a significant positive correlation between urinary and breast milk Cd concentrations. They concluded that maternal Cd exposure led to an increased risk of premature delivery and low birth weight.

Research continues on *metallothionein isoforms and Cd speciation*. Alvarez-Llamas *et al.*[33] reported a method for the separation of rabbit liver metallothionein isoforms using CZE

and UV detection. The authors investigated the effect of experimental conditions including buffer composition, ionic strength and separation voltage on the resolution of the metallothionein species. The eluent from the electrophoresis unit was directly introduced to an ICP-mass spectrometer for quantitative determination of Cd in the separated metallothionein isoforms. The CZE-ICP-MS method was also used to determine Cd in metallothionein separated from hepatopancreas cytosol of mussels kept in a metal rich environment.

Finally, in a very interesting application of ETAAS, Wang and colleagues[92] developed a *novel sandwich type immunoassay method* for the quantitative determination of α-fetoprotein (AFP) in human serum, which used an EDTA–Cd chelate labelled streptavidin and biotinylated antibody. Assays were performed in standard 96-well microtitre plates which acted as the solid phase carrier. After binding of the streptavidin-chelate to the antigen–antibody complex and washing of the plate to remove excess unbound reagent, the bound Cd was dissociated from the immune complex by addition of 0.2 M HNO_3 to each well. The dissociated Cd was determined by ETAAS to indirectly quantify the antigen concentration. Concentrations of AFP were determined in 23 human serum samples using this metal chelate method and compared with results obtained by a fluoroimmunoassay method. A good correlation (r = 0.993) was observed between the two methods.

1.9.7 Calcium. Burguera *et al.*[78] investigated *the relationship between sex, age and concentration of Ca and Sr in different bone types.* Bone samples, taken during surgery to repair fractures to normal and osteoporotic bone, were acid digested and concentrations of Ca and Sr determined by FAAS using a N_2O–C_2H_2 flame. Coefficients of variation for bone Ca and Sr were greater than 40%, reflecting the great heterogeneity in the data. The authors reported that many women had low mineral levels in bone samples and also that there was a decrease in the concentration of both elements in bone samples from men aged over 55 years and women aged over 45 years. In the different bone types examined, they observed lower element levels in the femur head, which they suggested was due to a preferential demineralisation of this bone type.

Sturup[31] described a *novel method for the determination of total Ca and Ca isotope ratios in urine using double focusing SF-ICP-MS* with a shielded torch. The method was used to determine ^{44}Ca:^{43}Ca, ^{41}Ca:^{43}Ca and ^{44}Ca:^{42}Ca ratios in nutritional studies of Ca absorption using enriched stable isotopes. The three isotope ratios were determined with precisions of 0.25%, 0.25% and 0.05%, respectively. The author considered that the overall uncertainty calculation for a double stable isotope study (administration of enriched ^{42}Ca and ^{44}Ca) was mainly controlled by the precision of the measurement of the isotope ratios, whilst for a mixed stable and radioisotope procedure (administration of ^{44}Ca and ^{47}Ca) overall uncertainty in measurement was mainly influenced by the measurement of total Ca by isotope dilution.

1.9.8 Chromium. Isobaric interferences can severely affect the accurate determination of ultratrace levels of Cr in biological matrices. Chang and Jiang[32] developed a method for the determination of Cr in water and urine using ICP-MS equipped with a dynamic reaction cell (DRC). The researchers reported a *2–3 orders of magnitude reduction in the intensity of polyatomic ion interferences* on the quantitative determination of ^{52}Cr and ^{53}Cr by introducing a 1 ml min^{-1} flow of NH_3 into the DRC. With this approach, the authors reported LODs of 0.015 ng ml^{-1} and 0.024 ng ml^{-1} for ^{52}Cr and ^{53}Cr, respectively. The method was validated by analysis of riverine water and urine CRMs, using both external calibration and ID methods for quantification.

In this review period, a number of groups have been interested in the *release of elemental ions from orthodontic materials.* Agaoglu *et al.*[135] determined the concentrations of saliva and serum Cr and Ni in patients with fixed orthodontic appliances using ETAAS. Salivary concentrations of both Cr and Ni reached a peak in the first months of fitting of the appliance and then declined, whilst statistically significant increases in serum Cr and Ni were measurable only in the second year following fitting. The authors concluded that the orthodontic fittings did release measurable amounts of both elements but both Cr and Ni did not reach toxicologically important levels in either saliva or serum.

Ezer *et al.*[89] described a novel method for the quantitative determination of *Cr in water and biological fluids using ETA-LEAFS.* A tunable dye laser was used to excite Cr at 236.471 nm and fluorescence was measured at 302.2 nm or 357.9 nm. Samples were atomised from the wall of a pyrolytically coated graphite tube in a conventional graphite furnace using an ashing temperature of 1300 °C and an atomisation temperature of 2500 °C. The LOD was reported to be 4 pg ml^{-1} for a 20 μl injection volume. The authors used the method to determine Cr in serum samples and gastrointestinal perfusate following a 1 + 49 v/v and 1 + 1 v/v dilution, respectively, with deionised water. They also investigated the use of $Mg(NO_3)_2$ and Triton X-100 as chemical modifiers for quantitative determination of Cr in these matrices.

Rukgauer and Zeyfang[136] determined the concentration of *Cr in different blood cell populations* from healthy blood donors and diabetic patients using ETAAS. Different blood cell populations were separated from whole blood by density centrifugation. Concentrations of Cr were higher in plasma (248%), erythrocytes (61%) and platelets (91%) of the diabetic patients compared with blood donors, whereas Cr concentrations in polymorphonuclear and mononuclear leucocytes were 35% lower. The authors hypothesised that the high plasma Cr levels in the diabetic patients might explain the increased renal losses of Cr in diabetes, whilst the decreased lymphocyte levels could reflect a decreased body burden of Cr.

1.9.9 Cobalt. Sant'Ana *et al.*[8] described *a novel approach for the determination of Co in biological matrices using solid phase extraction with polyurethane foam.* The Co was extracted from an aqueous solution into the polyurethane foam as a Co–SCN complex. The foam sample was inserted into the graphite tube of an electrothermal atomiser for determination of Co. The polyurethane foam was completely pyrolysed using an ashing temperature of 550 °C and Co was determined quantitatively without the addition of any chemical modifier. Calibration was with aqueous standards. The method was validated by analysing biological CRMs.

1.9.10 Copper. Ji and Ren[84] reported significantly improved sensitivity for the determination of Cu and Zn in human serum using *derivative FAAS* with a micro-sample introduction system. Using a sample volume of 100 μl, the authors reported LODs of 0.015 μg ml^{-1} and 0.008 μg ml^{-1} for Cu and Zn, respectively, which were 4.5–6.5 fold better than LODs achieved by conventional micro-sampling FAAS.

Camero *et al.*[137] developed a method *for the quantitative determination of Cu in human seminal plasma using ETAAS.* Untreated seminal plasma samples were introduced into the graphite tube with a tungsten probe, which also acted as the atomisation surface. This sample introduction method was compared with one involving acid digestion and introduction using an autosampler. The authors reported more than a three-fold improvement in sensitivity using the tungsten probe method (2.4 pg with probe *versus* 8.2 pg for digested sample). However, they noted that non-heterogeneous Cu distribution in the undigested sample affected reproducibility, which could be improved by ultrasonic treatment of the sample prior to analysis. Lima and colleagues[138] also described a method for the determination of Cu in biological matrices using

ETAAS. The integral platform of the graphite tube atomiser was coated with a Rh–W mixture, which acted as a permanent chemical modifier. The authors reported that this was as effective as a conventional Pd–$Mg(NO_3)_2$ chemical modifier for the thermal stabilisation of Cu in both digested and slurry samples and remained effective for 250–300 atomisations. Furthermore, they noted that there was less variability in the calibration slope throughout the lifetime of the tube, thereby lessening the requirement for recalibration.

Romero *et al.*[139] used FAAS to determine *Cu and Zn concentrations in serum from representative populations of the Canary Islands*. Reported mean Cu and Zn concentrations were 1.10 mg l^{-1} and 1.16 mg l^{-1}, respectively, which were comparable with values reported for other Spanish regions. However, individuals from Lanzarote had higher serum Cu and Zn levels compared with the rest of the islands, which the authors attributed to geological or dietary differences. Serum Cu concentrations were observed to vary with age, with highest Cu levels found in 20–30 year olds. No influence of age on serum Zn levels was observed.

In an interesting study to improve sampling methods for monitoring whole body exposure to toxic substances, Wheeler and Warren[140] described a standardised approach to measure contamination over the entire coveralls of workers applying Cu based biocides. Copper contamination on selected areas of coveralls was determined using portable XRF and the total body exposure estimated by averaging, based on Dirichlet tessellation of the measurement locations. This approach was compared with a more conventional patch sampling method and whole suit digestion as the benchmark reference method. Mean absolute percentage error for the tessellation method varied between 0% and 20% with the benchmark method. However, the authors argued that the tessellation method gave much better spatial resolution than either the whole suit or patch test methods and that this detailed information on patterns of deposition was very valuable for chemical risk assessment. Flores and colleagues[85] described a new *direct solid sampling device for the determination of Cu in bovine liver using FAAS*. A sample of freeze-dried bovine liver RM, between 0.05 and 0.5 mg, was weighed into a small polyethylene vial which was connected to a glass chamber. The sample was transported in air as a dry aerosol into a quartz T-cell positioned immediately above the flame of the spectrophotometer. The transient Cu absorbance signal was integrated over a 3 s period for quantitative determination of Cu in the sample. The results obtained by this method were in good agreement with the certified value and with results obtained using acid digestion of samples and conventional solution nebulisation FAAS.

1.9.11 Lead. *Lead continues to be one of the major elements of interest in relation to environmental and occupational exposures.* Grinberg and de Campos[88,141] described a method for the determination of Pb in whole blood, urine and biological tissues by ETAAS, in which Ir coating of the graphite tube was used as a permanent chemical modifier. The coating was sufficient for up to 1100 firings without loss of analytical sensitivity. Blood and urine samples were diluted with 0.2% HNO_3–0.1% Triton X-100 and matrix matched standards were used for calibration. The method was validated by analysing a range of CRMs and commercial quality control materials. Zhou *et al.*[87] investigated the use of Rh as a permanent chemical modifier for the determination of Pb in biological fluids using ETAAS with a tungsten filament atomiser and self-reversal background correction. The filament was simply conditioned with an Rh solution to provide a permanent coating for the determination of Pb in whole blood and urine matrices. The authors noted that the Rh coating not only stabilised Pb during the ashing stages but also improved the removal of carbonaceous residue during the clean-up phase, thereby extending the filament lifetime beyond 300 firings. Aqueous standards were satisfactory for the determination of Pb in whole blood, but for the quantitative determination of Pb in urine, matrix matched calibration standards were necessary. Reported LODs were 1.5 μg dl^{-1} and 27 μg l^{-1} for blood and urine, respectively. The method was validated by analysing CRMs and samples from proficiency testing schemes.

Parsons *et al.*[94] described the *preparation and validation of RMs* for the determination of Pb in blood and urine. Four candidate materials of each matrix type, containing Pb at clinically relevant concentrations, were distributed among 21 specialised laboratories. The laboratories used ASV, ETAAS and ICP-MS to determine concentrations of Pb in the samples. The results from two interlaboratory comparison exercises were used to assign 'certified' values and uncertainty estimates for these RMs. The authors noted that certification of the urine RM proved troublesome, particularly at concentrations above 600 μg l^{-1}. Fast portable techniques for the determination of blood Pb have become commercially available, potentially taking analysis out of the specialised laboratory and to the 'point of care'. Pineau and colleagues[142] compared the analytical performance of a portable blood Pb analyser, the Leadcare system, with a validated method using ETAAS. An overall correlation coefficient of $r = 0.95$ between the methods was reported for the analysis of 76 samples from occupationally exposed workers. The authors considered that the Leadcare system was satisfactory for initial screening purposes, but cautioned that the system required unfrozen samples collected less than 24 h before analysis.

Haraguchi *et al.*[143] used ETAAS to determine concentrations of Pb in fresh-frozen and formalin-fixed brain tissue of subjects with diffuse neurofibrillary tangles with calcification (DNTC), a form of presenile dementia. The researchers reported higher Pb levels in DNTC brain tissue and hypothesised that Pb neurotoxicity might be involved in the pathogenesis of DNTC. Erfurth *et al.*[144] investigated the effect of Pb exposure on the endocrine system in groups of active and retired lead smelter workers. Whole *blood and plasma Pb concentrations* were determined using ETAAS and ICP-MS. Finger bone Pb levels were determined using K-XRF. Levels of pituitary and thyroid hormones in serum were determined by immunoassays. One sub-group of workers and a corresponding control group were challenged with gonadotrophin- and thyrotrophin-releasing hormones and stimulated levels of pituitary hormones were measured. For the non-challenged group, the authors observed no significant association between blood, plasma or bone Pb concentrations and the measured hormones. However, in the challenged group they reported significantly reduced levels of follicle-stimulating hormone. They concluded that moderate exposure to Pb was associated with only minor changes in male endocrine function, particularly the hypothalamic–pituitary axis. Sonmez *et al.*[145] investigated the effect of chronic low level Pb exposure on renal tubular function in a group of teenage workers in an auto-repair shop. Blood lead levels were determined by AAS and urinary *N*-acetyl-β-glucosaminidase (NAG), a marker of renal tubular damage, was determined by a colorimetric method. Levels of blood Pb and urinary NAG were compared with a non-exposed control population and a group of adult lead battery workers. The mean blood Pb level in the adolescent workers was 8 μg dl^{-1}, which was higher than the control group (3.49 μg dl^{-1}) but significantly lower than the battery workers (25.3 μg dl^{-1}). Urine NAG was also significantly higher in the youths than in controls (4.71 U g^{-1} creatinine *versus* 3.07 71 U g^{-1} creatinine). The authors concluded that chronic low-level Pb exposure was associated with early renal tubular damage in the young workers. Smith and colleagues[146] studied the longitudinal relationship between blood and plasma Pb in a group of women of reproductive age living in Mexico City. Samples were taken using a 'metal-free' sampling technique and levels of Pb

in both whole blood and plasma determined by HR-ICP-MS. Repeat blood samples were taken from a subset of the study population, either weekly for a four week period or monthly over a 9 month period. The authors reported a positive curvilinear relationship between plasma and blood Pb over the measured blood Pb concentration range (2.13–39.7 μg dl^{-1}). They noted that the within-subject and between-subject variance components were not statistically significantly different between the short term repeat sampling and long term repeat sampling sub-groups. They reported that the relative partitioning of Pb between whole blood and plasma naturally varies by 2–4 fold at a given blood Pb concentration. They concluded that measurement of plasma Pb may be used clinically, providing 'trace-metal clean' sampling procedures are used.

Rahman *et al.*[77] studied chronic Pb exposure in children from Karachi by determining *Pb levels in deciduous teeth* using ETAAS. A total of 309 teeth were collected from children at nine primary schools in the Karachi region. The Pb levels ranged from 0.42 μg g^{-1} to 39.7 μg g^{-1} with a mean value of 5.78 μg g^{-1}. Incisors had significantly higher levels of Pb than either molars or canine teeth. Significant variation was also observed in the levels of Pb in teeth taken from children at the different schools. In another study, Tsuji *et al.*[147] used ETAAS to determine Pb levels in dentine chips taken from exfoliated deciduous teeth of First Nation school children in a remote region of northern Ontario. The group reported a mean Pb concentration of 9.2 μg g^{-1} and found no difference in Pb concentrations between different tooth types. What is of interest to this reviewer is the observation that the levels determined in this remote population are similar to those reported for children from urban environments, although the sources of Pb exposure may be quite different. In this case the exposure source was hypothesised to be from Pb contaminated wild game, which still constitutes an important food source for this population.

This review period has again seen *much activity in the* in vivo *determination of bone Pb by XRF*. As part of a US normative ageing study, Elmarsatawy *et al.*[54] investigated the risk factors for elevated bone Pb in relation to occupation. The researchers determined bone Pb and blood Pb levels in 656 American workers using K-shell XRF and ETAAS, respectively. Subjects were categorised into white collar or blue collar workers and none had been engaged in a primary lead industry. A multivariate regression model, which adjusted for confounding factors, showed blue collar workers to have tibia and patella bone Pb levels respectively 5.5 μg g^{-1} and 6.5 μg g^{-1} higher than white collar workers. Tibia and patella Pb levels were even higher in non-white blue collar workers. The authors concluded that bone Pb levels are higher in blue collar workers even if they have not been occupationally exposed to Pb. Gomaa *et al.*[148] determined maternal bone Pb and umbilical cord blood Pb levels in a study to investigate risk factors for infant mental development. Maternal tibia and patella bone Pb concentrations were measured in 197 women, within 4 weeks of giving birth, using K-shell XRF. Umbilical cord blood Pb concentrations were determined by ETAAS. After adjusting for confounding factors, the authors reported that Pb levels in both umbilical cord blood and trabecular bone were significantly and independently inversely associated with the Bayley mental development index scores. They concluded that high maternal trabecular bone Pb levels are an independent risk factor for impaired mental development in very young infants. They attributed the effect to mobilisation of maternal Pb bone stores. The study of Tellez-Rojo *et al.*[53] is particularly pertinent to this previously described study. They investigated the hypothesis that lactation stimulates release of bone Pb. The group determined tibia and patella Pb levels using K-shell XRF. Blood samples were collected from 425 lactating women at delivery and at 1, 4 and 7 months *post partum*. Pb concentrations were determined by ETAAS. The mean blood Pb level at delivery was 8.4 μg dl^{-1} and mean cortical and trabecular bone Pb levels were 10.6 μg g^{-1} and 15.3 μg g^{-1}, respectively. The authors estimated that women who exclusively breast fed had blood Pb levels that were increased by 1.4 μg dl^{-1} in relation to those who had stopped and concluded that their findings supported the hypothesis that amount of Pb released from bone is directly related to lactation. Finally, Todd and colleagues[45,46,50,51,91] presented a highly relevant series of papers in which they sought to validate the *in vivo* measurement of Pb in bone using K-shell and L-shell XRF. The group measured tibia bone Pb concentrations in intact and dissected human cadaver legs using both techniques. They compared the XRF results with results obtained by ETAAS, following acid digestion of samples taken from the same regions of the tibia. The authors reported the following key observations. Surface Pb concentrations were approximately 5 μg g^{-1} higher than core Pb concentrations in bones with a low Pb content and approximately 8 μg g^{-1} higher in bones with a high Pb content. Core tibia Pb concentrations determined by ETAAS ranged from 3–19 μg g^{-1} compared with values of 2–35 μg g^{-1} determined by K-shell XRF. No significant difference was observed in bone surface Pb concentrations determined by the two techniques but XRF significantly overestimated core tibia Pb concentrations. Agreement between tibia Pb concentrations measured by L-shell XRF and ETAAS was good when XRF measurements were made on bare bones but poor for XRF measurements made on intact legs. They considered all these observations had important consequences for non-invasive bone measurements. Indeed they expressed considerable concern over the use of L-shell XRF for bone Pb measurements.

1.9.12 Manganese. Torra and colleagues[149] used ETAAS to determine serum Mn levels in healthy subjects, aged between 15 and 90 y, from Barcelona. *The authors established a Mn 'reference' interval of 0.3 μg l^{-1}–2.5 μg l^{-1}, with a 95th percentile value <1.8 μg l^{-1}.* They observed no significant relationship between serum Mn concentration and gender, but noted that serum Mn levels were nearly three times higher in the younger than in the older population. Corriera *et al.*[70] described a method for the simultaneous determination of Mn and Se in serum using simultaneous ETAAS. Serum samples were simply diluted 1 + 3 v/v with 1% HNO_3–0.1% Triton X-100 and both Pd and $Mg(NO_3)_2$ were added as chemical modifiers. The authors noted that injection of 15 μl of an oxidant mixture (H_2O_2–HNO_3) immediately after the drying step, and a low ashing temperature of 400 °C, markedly reduced the build up of carbonaceous residue in the graphite tube. The LODs for a 15 μl injection volume were reported to be 6.5 pg and 50 pg for Mn and Se, respectively.

1.9.13 Mercury. This review period has seen considerable activity in the development of methods for the determination of total Hg and Hg species in a variety of biological matrices. Gelaude *et al.*[150] described a solid sampling method for the determination of inorganic Hg and methylmercury in biological samples by ETV-ICP-MS. The authors considered *the solid sampling approach had many advantages in that contamination risks and analyte losses were kept to a minimum* and, most importantly, the chemical forms of Hg were maintained in their original state within the sample. Solid samples were introduced into a 'boat-in-tube' graphite furnace and heated to sequentially vaporise methylmercury and inorganic Hg. Quantitative determination of the Hg peaks was achieved using ID with isotopically enriched ^{200}Hg in a stable argon flow, generated using an 'in-house' manufactured permeation tube. Dressler *et al.*[151] developed a method for the determination of total Hg in blood and urine using CV-AAS, with on-line separation and pre-concentration of the analyte. Blood and urine samples were

microwave digested in closed vessels using HNO_3–$HClO_4$. The digested sample was complexed with *O,O*-diethyldithiophosphoric acid (DDTP) and adsorbed onto a silica C_{18} column. The complexed Hg was subsequently eluted from the column with CH_3OH and reacted 'on-line' with $NaBH_4$ for quantitative determination by CV-AAS. The authors described optimum conditions for 'on-line' pre-concentration and cold vapour generation. The reported LOD was 20 ng l^{-1} and a sample throughput of 24 samples h^{-1} was achieved. The method was validated by analysing a urine CRM and spiked blood samples. Bettinelli and colleagues[152] also described a method for the determination of total Hg in urine using FI-CV-ICP-MS. Samples were microwave digested 'on-line' using an oxidation mixture of KBr–$KBrO_3$ and final oxidation with $KMnO_4$. The reported LOD was 0.03 μg l^{-1}, which was an order of magnitude better than the LOD of 0.2 μg l^{-1} achieved using FI-CV-AAS. The authors reported quantitative recovery of phenylmercury chloride, dimethylmercury, mercury acetate and methylmercury chloride from spiked samples. They considered the method to be suitable as a 'reference method' for the determination of Hg in urine at the very low concentrations found in non-exposed subjects.

Three groups reported methods for the determination of *Hg in hair*. Wang *et al.*[153] investigated optimum conditions for the determination of total Hg in hair by CV-AAS. Hair was digested under pressure with HNO_3–H_2SO_4–H_2O_2. Mercury was reduced to Hg^0 with $SnCl_2$ for quantitative determination. Under the optimum conditions established, an LOD of 0.5 μg l^{-1} was reported. Results of the analysis of hair CRM gave values between 95% and 102% of the certified value. Morton *et al.*[96] determined both inorganic Hg and methylmercury in human hair using HPLC coupled to ICP-MS. Hair samples were cold digested with HNO_3–H_2O_2 (2 : 1 v/v) and a minimum mass of 100 mg was required for accurate quantitative determination. The authors investigated the effectiveness of different washing procedures to remove exogenous contamination and established that soaking hair with a simulated sweat solution followed by washing with 0.1 M HCl was effective at removing methylmercury from hair. Diez and Bayona[102] described a method for the determination of Hg species in human hair using GC-CVAFS. Following acid digestion the Hg species were ethylated and extracted from the digest by headspace solid-phase micro-extraction for quantitative determination by GC-CV-AFS. The authors presented optimised conditions for ethylation, extraction and chromatographic separation. They reported LODs of 50 ng g^{-1} and 80 ng g^{-1} for methylmercury and Hg^{2+} species, respectively, in a 100 mg sample. The method was validated by analysis of an NIES hair CRM.

Rodil and colleagues[154] also coupled *solid-phase micro-extraction with GC for quantitative determination of methylmercury in biological matrices by MIP-AES*. In their method, biological samples were microwave digested with 3 M HCl followed by derivatisation and solid-phase micro-extraction on a silica capillary column coated with polydimethylsiloxane. Optimum conditions for derivatisation and extraction were pH 5, 100 °C and 15 min sorption time. The method was validated by analysing a range of biological CRMs. Dietz *et al.*[155] described a similar sample separation technique for the determination of Hg species by MIP-AES. Microwave digested samples were derivatised for cryogenic trapping and GC separation on the same capillary column. The derivatisation, trapping and chromatographic steps were semi-automated and regulated by a control unit developed by the researchers. Reported LODs for the Hg species dimethylmercury, methylmercury and ethylmercury were 6 ng l^{-1}, 0.95 ng l^{-1} and 1.25 ng l^{-1}, respectively. A complete analytical cycle was 15 min. The method was validated by analysing the CRM BCR 710 and was used to determine Hg species in a range of marine biological materials. A second Spanish group, da Rocha *et al.*,[156] described a method for the separation and determination of Hg species using CE and generation of volatile species with detection by ICP-MS. Inorganic Hg, MeHg and ethylmercury species were separated as Hg–cysteine complexes on a fused silica capillary using a sodium tetraborate dodecahydrate buffer. Separated species were reacted on-line with $NaBH_4$ and detected using either quadrupole or double focusing SF-ICP-MS. LODs in the low μg l^{-1} range were reported for the Hg species. The method was evaluated by analysing the CRM DOLT-2.

Ramalhosa *et al.*[157] described a rapid alkaline microwave digestion sample preparation procedure for the determination of *methylmercury in biological samples by HPLC-CV-AFS*. Samples were microwave digested in a methanolic KOH solution and subsequently reacted with CH_2Cl_2 to reduce matrix interference effects on the determination of methylmercury. Elimination of matrix interferences was checked by comparing the slope of aqueous calibrations with standard additions calibration. The LOD for the method was 10 μg kg^{-1} and the RSD was <8% for methylmercury concentrations between 0.15 and 3 mg kg^{-1}. Good agreement with certified values were reported for two marine biological CRMs.

The research group of Ask *et al.*[158] investigated levels of inorganic Hg and methylmercury in placentas of Swedish women. They determined Hg concentrations in placental tissue and maternal and cord blood from 110 women using alkaline solubilisation and reduction of samples with quantification by CV-AFS. The authors observed that *placental levels of inorganic Hg increased with increasing number of dental amalgam fillings*. They also noted that methylmercury accumulated in the placenta and that, on average, 60% of placental Hg was in the methylated form. The median placental concentration of methylmercury was 1.8 μg kg^{-1} which was twice the maternal blood methylmercury level. They reported a significant association of Hg and Se in maternal and umbilical cord blood but not in placenta tissue. Zimmer and colleagues[159] used CVAAS to determine concentrations of Hg in blood, urine and saliva in one group of women who had self-reported ill health effects arising from amalgam fillings ('amalgam sensitive' subjects) and a second control group with no reported ill health effects. Median blood and urine Hg levels in the 'amalgam sensitive' group were 2.35 μg l^{-1} and 1.55 μg l^{-1}, respectively, compared with values of 2.4 μg l^{-1} and 1.8 μg l^{-1} in the control group. All measured blood and urine Hg levels were considered to be in the reference range for the general population. Saliva Hg concentrations did not correlate with either blood Hg or urine Hg concentrations and the authors concluded that saliva Hg determination was not suitable for biological monitoring. Finally, Apostoli *et al.*[160] described the results of a polycentric study to establish a reference value for Hg in urine for an Italian population. Subjects were selected on standardised criteria including dietary habits, lifestyle, exposure history and number of dental amalgams. Urine Hg was determined by CVAAS and FI-ICP-MS. The median values (5%–95% percentile values) were reported to be 0.78 μg g^{-1} creatinine (0.17–3.66 μg g^{-1} creatinine) using CVAAS and 0.79 μg g^{-1} creatinine (0.12–5.02 μg g^{-1} creatinine) using ICP-MS. The reference value reported was lower than values reported previously, which the authors considered to be due to the selection criteria used for the reference population and the control of pre-analytical and analytical factors of variability.

1.9.14 Molybdenum. Minoia and colleagues[161] developed a method for the determination of Mo in urine using ICP-MS. Samples were simply diluted in distilled H_2O–1% HNO_3 and both In and Y added as internal standards. The authors evaluated factors such as sample dilution, acid concentration and analyte stability for the method. Selecting ^{98}Mo as the measured isotope, an LOD of 0.2 μg l^{-1} was reported and

calibration was linear from 2–50 μg l^{-1}. The authors used the method to establish a reference value for Mo in urine of an Italian population. Sievers *et al.*[162] used ETAAS to monitor urinary excretion of Mo in infants. The authors compared different urine collection methods (catheterisation, random midstream samples and urine collection bags). Samples collected by catheterisation had a mean Mo concentration of 7 μg l^{-1} (0.5–60.1 μg l^{-1}), whilst a mean Mo concentration of 21.25 μg l^{-1} (0–91 μg l^{-1}) was quoted for midstream and collection bag samples. They also investigated *diurnal variation of Mo excretion in preterm infants fed either human milk or infant formula.* They concluded that although the diurnal variation observed was of minor clinical significance it should be accounted for by defining sample collection times and urine reference values. The same group[163] used both ETAAS and ICP-MS to study Mo metabolism in infancy. Premature infants with a post-natal age of between 10 and 54 d were given 25 μg ^{100}Mo kg^{-1} in a human milk or infant formula feed. Fecal and urine samples were collected both immediately preceding and for 72 h following administration of the label, for determination of Mo. Median absorption of Mo was 97.5% and retention of nutritive Mo intake was 35.7%. Peak urine Mo concentration was determined within 8 h of administration. The authors considered that orally administered Mo was well absorbed in premature infants and that dietary recommendations for Mo should prevent excessive intakes.

Burguera *et al.*[164] conducted a *comprehensive evaluation of chemical modifiers* for the determination of Mo in whole blood using ETAAS. They reported that the most sensitive and reproducible determinations of Mo were obtained using an Er chemical modifier (25 μg) added to whole blood samples diluted 1:2 v/v with 0.1% Triton X-100. The build up of carbonaceous residue in the graphite tube could be minimised by injecting 20 μl of 15% H_2O_2 and running the temperature programme after every five analyses. An LOD of 0.6 μg l^{-1} and an RSD of 0.8–1.5% were reported.

1.9.15 Nickel. Todorova *et al.*[165] described methods for the determination of Ni in serum and urine using ETAAS. The method used an *H_2O_2 chemical modifier to assist thermal decomposition of the protein matrix.* Optimum atomisation temperatures were reported to be 2100 °C and 2200 °C for serum and urine, respectively, and calibration was performed with aqueous Ni solutions containing glycine. The reported LODs were 0.2 μg l^{-1} for both biological matrices and RSDs were 8–15% for Ni concentrations between 0.5 and 2.5 μg l^{-1}. Soylak[166] developed a method for the determination of Ni in water and urine in which Ni was separated and preconcentrated by adsorption on Dialon HP 20 resin as a 1-nitroso-2-naphthol-Ni complex. The authors reported optimum conditions for chelation and adsorption of Ni onto the resin. Adsorbed Ni was eluted from the resin using 1 M HNO_3 in acetone for determination by FAAS.

The group of Hostynek and colleagues reported the findings of a series of studies on the permeation of Ni ions through the human stratum corneum. In vitro *permeation was investigated in an advanced diffusion cell system using trypsinised stratum corneum from cadaver leg skin.*[167] One per cent. aqueous solutions of $Ni(NO_3)_2$, $NiSO_4$, $NiCl_2$ and $Ni(CH_3COO)_2$ were applied as the donor solutions. Concentrations of Ni in donor fluid, receptor fluid and in the stratum corneum were determined using ICP-MS. Over a 96 h incubation period, only 1% of the applied dose was recovered in the receptor fluid and a further 1% retained in the stratum corneum. The authors noted that the calculated permeability coefficient of 5.2–8.5 × 10^{-7} cm h^{-1} was similar to values previously reported for full thickness skin studies. They hypothesised that, *in vivo*, Ni ions may permeate human skin simultaneously by both intercellular and transcellular routes and shunt pathways. The group also examined *in vivo* penetration of Ni salts in human stratum corneum using a sequential tape stripping technique.[168] The same four Ni salts as used in the *in vitro* study were applied in a methanol solution to the arm and back. Exposed areas of skin were stripped 20 times, to the glistening layer, and the Ni content of each strip determined using ICP-AES. The researchers observed that, for incubation periods up to 24 h, most of the Ni dose remained on the skin surface or adsorbed into the uppermost layer but at high concentrations Ni salts appeared to penetrate beyond the stratum corneum. In the case of $Ni(NO_3)_2$, low but constant measurable levels of 1% of the applied dose were determined in layers beyond the third tape strip suggesting intercellular diffusion for Ni and NO_3^{2-} counter ions. The authors noted that arm skin was more permeable to Ni than back skin and concluded that the Ni counter ion was important in influencing Ni diffusion. In addition to the *in vivo* study of skin penetration of soluble Ni salts, the researchers examined the diffusion of Ni in stratum corneum following occlusive application to the forearm of Ni metal powder.[169] The same tape stripping approach was used as in the previous paper.[168] The Ni content of the 20 successive strips was determined by ICP-AES. The gradient of Ni distribution in successive layers increased proportionally with the length of time of application of the powder up to the tenth strip layer and then remained constant in the subsequent 10 layers. The authors concluded that Ni metal powder in contact with skin was oxidised to form a soluble species, which could penetrate the intact stratum corneum and thus had the potential to elicit an allergic reaction.

Other researchers have investigated the *release of Ni from biomedical implants and dental casting alloys.* Wataha *et al.*[170] used LA-ICP-MS to examine the spatial localisation of solubilised Ni around Ni containing implants. Following subcutaneous implantation of pure nickel wire, a nickel–chromium alloy wire or polyethylene (as a inert control material) in mice, tissues were analysed for inflammation at 1 mm intervals from the implantation site and levels of Ni quantitatively determined using a laser ablation technique. In the case of polyethylene implantation, mild inflammation was noted up to 1–2 mm from the implantation site. There was severe inflammation with the pure nickel wire implant, whilst the nickel–chromium alloy produced inflammation similar to that of the polyethylene implant. Levels of tissue Ni reached 48 μg g^{-1} close to the nickel wire implant but were less than 4 μg g^{-1} in the tissue close to the alloy implant. The authors concluded that Ni distribution around the implant site correlated well with overt tissue inflammation.

1.9.16 Platinum and noble metals. Yang and colleagues[171] presented a *comprehensive review of sensitive techniques for the determination of Pt in body fluids and tissues.* The review covered sample preparation procedures, analytical figures of merit for different instrumental techniques and specific clinical applications. Da Silva *et al.*[172] employed the phenomenon of cloud point extraction for the determination of noble metals, including Au, Ir, Pt and Rh, in biological matrices. Biological samples were acid digested and the digest solution reacted with *O,O*-diethyldithiophosphate and Triton X-114. Raising the temperature of the solution to the cloud point led to a two-phase separation in which the noble metals were complexed in the surfactant-rich phase. Noble metals in this phase were quantitatively determined by ETV-ICP-MS. This approach gave enrichment factors ranging from 7 for Rh to 60 for Pt and LODs from 0.6 ng l^{-1} for Pt to 3 ng l^{-1} for Rh. The authors noted that efficient complexation and extraction into the surfactant phase was only achievable for urine samples following complete acid mineralization of the urine matrix.

Many of the papers on the determination of Pt in this review period continue to report on the determination of total Pt and Pt species in tissues and body fluids for studies on the pharmacokinetics of a variety of Pt containing therapeutic

drugs. Tibben *et al.*[173] used ETAAS to determine total Pt in plasma and plasma ultrafiltrate from patients administered AP5280, a Pt containing *N*-(2-hydroxypropyl)methacrylamide copolymer. Samples were simply diluted 1 + 4 v/v with 0.2 M HCl and an LOQ of 0.25 μmol l^{-1} was reported. Verschraagen *et al.*[174] developed a sensitive method for the quantitative determination of cisplatin and its major metabolite, monohydrated cisplatin, in plasma from patients administered the drug to treat solid tumours. Cisplatin and monohydrated cisplatin were separated by HPLC and determined separately 'off-line' by ETAAS. Limits of quantification for the two species were 60 nM and 82.5 nM for cisplatin and the monohydrate metabolite, respectively. Suzuki *et al.*[67] used TXRF to determine trace levels of cisplatin in biopsy samples of cancerous tissues. Using a monochromatic Mo Kα-radiation source and LiF crystal, an LOD of 0.1 ppm was reported. The authors used the method to monitor serum and tissue Pt concentrations over time in patients with bladder cancer who were administered the drug. Pascual *et al.*[175] reported the results of a very important study to improve the placental impermeability to cisplatin for therapeutic treatment during pregnancy. Cisplatin was coupled with a bile acid to produce the modified drug Bamet-R2. Following intravenous administration of either cisplatin or Bamet-R2 to pregnant rats, blood and tissue samples were acid digested and Pt determined by ETAAS. The authors reported much lower levels of Pt in foetal tissues from rats administered the modified drug and also noted that placental tissue levels of Pt were several fold higher in rats administered cisplatin. The authors concluded that the placental barrier is much more effective in protecting the foetus from cisplatin when the drug is coupled with a bile acid moiety. They highlighted the potential value of using the modified drug for treating tumours in pregnant patients. Carr *et al.*[176] investigated the *in vitro* biotransformation of a novel therapeutic Pt compound, satraplatin, in biological fluids using HPLC-ICP-MS. The researchers reported that satraplatin concentrations fell rapidly in fresh whole blood, with a half life of 6.3 min. In plasma and supplemented cell culture medium, however, the compound was much more stable and disappeared with half lives of 53 h and 22 h, respectively. They determined two Pt species in CH_3OH extracts from whole blood spiked with satraplatin, which were identified as the Pt^{II} complex JM 118 and a Pt-containing protein with an electrophoretic mobility similar to serum albumin. They also determined that at equilibrium, 62% of the Pt added to whole blood was bound to red cells and was not extractable with NaCl or CH_3OH. They concluded that satraplatin underwent rapid biotransformation in whole blood to the JM 118 complex, a protein associated fraction and a Pt fraction irreversibly bound to red cell membranes.

1.9.17 Rare earth elements. Blaum and colleagues[37] determined ultratrace levels of Gd in microsamples of tumour tissue using RIMS. An isotope specific detection limit of 1.5×10^9 atoms was reported, which corresponded to a total Gd detection limit of 1.6 pg based on the major ^{158}Gd isotope. The reported linear dynamic range was six orders of magnitude. The authors used the method to determine Gd levels in normal tissue and tumour tissue samples of mice administered an injection of the MRI contrast agent gadolinium diethylenetriaminepentaacetic acid dimeglumine (Gd-DTPA). They noted that the tissue Gd concentration could vary by two orders of magnitude depending on tissue type. Ortega *et al.*[6] *exploited cloud point precipitation, described earlier in the section on Pt, for pre-concentration of Gd from urine for quantitative determination by FI-ICP-AES.* Pre-concentration was performed on-line by complexing Gd with 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol in a non-ionic micelle system. The surfactant rich phase containing the Gd complex was retained on a micro-column packed with cotton and subsequently eluted with 4 M HNO_3 directly into the nebuliser of the ICP. The authors reported an enrichment factor of 20 for a 10 ml sample volume and the LOD was 40 ng l^{-1}. Analytical precision at a Gd concentration of 2 μg l^{-1} was 1.9% RSD.

Silva *et al.*[86] used AAS with a tungsten coil atomiser for the determination of Dy and Eu in sheep faeces as part of an animal nutrition study. Faeces samples were dried, ground and digested with HNO_3–$HClO_3$ for quantitative determination of the two elements. The method was evaluated by comparison with an established method using ETAAS. Whilst results for Eu were comparable by the two methods, the values determined for Dy differed significantly, which the authors attributed to the memory effects caused by carbide formation in the graphite tube. The tungsten coil atomiser had a lifetime of 200 firings, which the authors reported to be three times better than the lifetime of the graphite tube. Reported LODs for the tungsten coil method were 6.9 μg g^{-1} and 2.1 μg g^{-1} for Dy and Eu, respectively. Bettinelli *et al.*[177] described a *method for the determination of REEs in urine* using ETV-ICP-MS. Undiluted urine samples were injected into the graphite tube of the ETV together with Freon-23 as a chemical modifier, which was noted to reduce the atomisation temperature of the elements and also reduce the memory effect from the lanthanides. Reported LODs for REEs ranged from 1–10 ng l^{-1}. Standard additions calibration was considered necessary for quantitative determination. Levels of REEs determined in urine specimens from healthy volunteers were in the range of 5–20 ng l^{-1}.

In a similar approach to that described previously in the section on Cd,[92] Zhang *et al.*[91] coupled a *sandwich immunoassay procedure with ICP-MS* for the quantitative determination of thyroid stimulating hormone (TSH) in human serum. In a conventional immunosorbant assay approach, TSH was bound to immobilised anti-TSH antibodies in wells of a microtitre plate. The bound TSH was then complexed with a biotinylated monoclonal anti-TSH antibody and Eu–streptavidin. After washing to remove unbound reagents, complexed Eu was extracted by addition of 1% HNO_3 and quantitatively determined by ICP-MS. The measured Eu signals were directly proportional to the serum TSH concentration. The authors reported good correlation between results for TSH obtained by this method and those obtained with a radioimmunoassay method.

1.9.18 Selenium. *This review period has seen Se established as another primary element of interest, both in relation to its essential trace element role and its association with various disease states.* Zanao *et al.*[178] developed a method for the determination of Se in whole blood using ETAAS. A combined permanent Rh–W platform coating and a co-injection of $RhCl_3$ with the sample was used ensure thermal stability of Se at a maximum pyrolysis temperature of 1300 °C. Samples were diluted 1 + 4 v/v with 0.2% HNO_3–0.5% Triton X-100. The permanent coating improved tube lifetime by 200% when compared with a normal tube and use of a Pd–$Mg(NO_3)_2$ chemical modifier. Tsalev and colleagues[179] compared methods for the determination of Se in biological materials by ETAAS, using a Rh chemical modifier, by FI-HG-ETAAS and FI-HG-AFS. Two sample digestion methods were investigated. The first involved overnight soaking with HNO_3, followed by microwave digestion with HNO_3–H_2O_2 and reduction with 4.8 M HCl. The second employed overnight soaking with HBr–BrO_3^- followed by pressurised microwave digestion. The reported LOD for the direct ETAAS method was 6 μg l^{-1}. Methods were evaluated by analysing a range of biological samples with certified values for Se. Machat *et al.*[180] described a method for the determination of Se in serum using ICP-AES with conventional pneumatic nebulisation. Samples were digested under pressure with HNO_3 to reduce the matrix

interference of CN^- on the determination of Se. Residual interference was corrected mathematically. An LOD of 0.01–0.02 mg l^{-1} was reported and the method was evaluated by analysing a serum RM. Szoboszlai *et al.*[73] determined Se and Sn in human brain tissue using ETAAS with Zeeman-effect background correction and $Pd(NO_3)_2$ as a chemical modifier. The authors reported Se concentrations between 200 ng g^{-1} and 700 ng g^{-1} in the brain regions examined. Ogra *et al.*[181] identified the major metabolite of Se in rat urine using HPLC coupled with ICP-MS and tandem ESI-MS. The urine sample was treated to remove interfering Cl^-, Na^+ and urea on measurements by ESI-MS. The species had an M_r of 299 Da and contained a methylselenyl group, an acetyl group and at least two hydroxyl groups. It was identified as Se-methyl-*N*-acetyl-selenohexosamine.

Al-Kunani[182] investigated the *Se status* of women with a history of recurrent miscarriages using a case control study. Blood samples and scalp hair samples were collected from groups of women with one or more successful pregnancies and women with a history of repeated miscarriage. Selenium concentrations in the samples were determined by ICP-MS. The authors reported a significant reduction in hair Se in the recurrent miscarriage group compared with the controls (0.14 μg g^{-1} *versus* 0.34 μg g^{-1}) but no significant difference in serum Se levels. They concluded that there was evidence of Se deficiency in women with recurrent miscarriages but this did not represent a simple nutritional deficiency. Tan *et al.*[183] examined the relationship between Se status and gestational diabetes. Serum Se levels were determined by HG-AFS. The mean serum Se levels in pregnant women diagnosed with gestational diabetes mellitus was 0.063 mg l^{-1} compared with 0.074 mg l^{-1} in healthy pregnant women and 0.108 mg l^{-1} in healthy non-pregnant women. The authors suggested that Se supplementation should be considered for pregnant women, particularly those with gestational diabetes or impaired glucose tolerance.

Hol *et al.*[74] investigated urine Se excretion in individuals with mercury amalgam dental fillings. The authors examined a group self-reporting symptoms from dental amalgam toxicity, a healthy group with amalgam fillings and a control group with no amalgam fillings. Subjects were injected with the chelating agent 2,3-dimercaptopropane-1-sulfonate to stimulate metal excretion. Urine samples were collected over a 24 h period and urine Se concentrations determined by HG-AAS. The authors reported that individuals with amalgam fillings excreted less Se over 24 h (36.4 μg) than individuals without fillings (47.5 μg). They concluded that individuals exposed to low levels of Hg from dental amalgam excrete less Se than unexposed individuals. The same group[75] also examined blood Se levels in individuals reporting adverse health effects from dental amalgam using HG-AAS. They observed that blood Se levels were statistically significantly lower in subjects who claimed ill health symptoms from mercury fillings (119 μg l^{-1}) compared with healthy individuals with amalgam fillings (130 μg l^{-1}). They hypothesised that individuals with self-reported ill-health from amalgam might have a different Se metabolism to healthy individuals. Brookes *et al.*[184] reported the results of an important study to investigate the *relationship between plasma Se levels and the risk of developing prostate cancer*. The authors carried out a case control study on 148 men participating in the Baltimore longitudinal study of ageing, including 52 individuals diagnosed with prostate cancer. Plasma Se levels were determined by ETAAS. After correcting for years before diagnosis, body mass index, alcohol consumption and smoking history, the authors reported that higher plasma Se levels were associated with a lower risk of prostate cancer. They concluded that low plasma Se levels were associated with a 4–5 fold increased risk of prostate cancer.

Muntau *et al.*[181] reported *reference values for serum Se in infants and children*. The group determined serum Se levels in 1010 healthy children and 60 patients on a protein restricted diet. They reported a statistically significant age dependency on median serum Se levels in the healthy group. Serum levels decreased from 1 to 4 months (0.64–0.44 μmol l^{-1}), increased from 4 months to 1 year (0.44–0.62 μmol l^{-1}) and then remained constant from 1 to 5 y (0.9 μmol l^{-1}). Levels increased slightly again to reach a plateau between 5 and 15 y (0.99 μmol l^{-1}). Of the children on the restricted protein diet, 87% had serum Se levels below the 2.5% percentile value of the reference value. They considered the changes in Se status reflected nutritional changes.

1.9.19 Silicon. Klemens and Heumann[185] developed a method for the quantitative determination of trace levels of *Si in biological and clinical samples* using HR-ID-ICP-MS. Samples were spiked with a ^{30}Si enriched solution and microwave digested with either HNO_3 or a HNO_3–HF mixture. By using both digestion methods on duplicate samples, the authors were able to differentiate the HNO_3 soluble Si species from the poorly soluble Si fraction. They noted that the sensitivity of the method was strongly influenced by Si concentrations in the blank. The blank Si signal was minimised by using a PFA nebuliser and spray chamber together with a Si nitride torch. With this instrumental configuration, LODs were 0.15 μg g^{-1} and 0.2 μg g^{-1} for the HNO_3 and HNO_3–HF digestion methods, respectively, which were considered to be sufficiently sensitive for the quantitative determination of Si in almost all biological matrices. The authors considered that the method could be suitable for certification of Si concentrations in biological and clinical reference materials.

1.9.20 Strontium. Prohaska *et al.*[186] determined ^{87}Sr:^{86}Sr *isotope ratios in prehistoric human teeth* and bones using ICP-MS. The authors considered that *post-mortem* microstructural changes in bone, for example dissolving and recrystallisation, could result in erroneous results if normal invasive sampling with sample digestion and liquid nebulisation ICP-MS were used for the measurement of Sr. The researchers therefore developed a method using LA-ICP-MS for Sr isotope measurements on transverse bone cross-sections. Strontium isotope ratios were made with a precision between 0.1 and 0.2% RSD. With this approach they identified mineralised phases enriched in Rb, which had arisen exogenously. The researchers also measured Sr ratios in the enamel and dentine of teeth from a Neolithic individual. Bone and dentine Sr ratios were similar whilst the enamel Sr composition was significantly different. The authors hypothesised that the individual had migrated in early childhood.

1.9.21 Tellurium. Ha *et al.*[187] developed a method for the determination of *Te in urine using HG-AAS with derivative signal processing*. The authors investigated the influence of several analytical factors on the derivative absorbance values. They reported a characteristic concentration of 0.042 μg l^{-1} and an LOD of 0.26 μg l^{-1}, which were, respectively, 52 and 26 times better than values using conventional HG-AAS.

1.9.22 Thallium. Maurice *et al.*[97] described an ID-ETV-ICP-MS method for the direct determination of *Tl in human scalp hair*. Hair strands were embedded in pressure-hardening glue and sequential 10 mm segments cut for introduction into the ICP using a solid sample injector. This approach enabled the longitudinal distribution of Tl to be measured in hair samples from a Tl poisoned individual. The concentration of Tl in the root segment was 0.4 μg g^{-1}, falling to 0.01 μg g^{-1} at the end of the 20 cm hair strand. The reported LOD was 0.7 pg, corresponding to a Tl concentration of about 5 ng g^{-1} for a 150 mg hair sample. The authors also compared the influence of different hair washing procedures on the analytical results.

Table 1 Analysis of clinical and biological materials

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Al	Blood, urine	AA;ETA;L	Al accumulation and excretion patterns were investigated in newly employed workers as well as in relation to changes in airborne Al levels in an Al smelter	118
Al	Serum	AA;ETA;L MS;ICP;HPLC	Chemical speciation of Al in human serum was discussed and analytical methods were reviewed	116
Al	Serum, urine	AA;ETA;L	The platform was treated with 500 μg of Ru. The values for m_0 were 31 and 33 pg for Al in serum or urine, respectively, compared with 31 pg in 0.2% v/v HNO_3. Therefore calibration with aqueous standards was possible. RSD was <5% and LOD was 0.4 μg l^{-1}	115
Al	Teeth	AA;ETA;L	Mean Al concentration in 323 deciduous teeth was 0.58 ± 0.60 ppm dry weight. Al content was dependent on tooth type and dental status	117
Al	Tissue	AA;-;-	The onset of macrophagic myofasciitis, a condition characterized by muscle infiltration by granular macrophages and lymphocytes, was associated with intramuscular injection of $Al(OH)_3$-containing vaccines. Symptoms appeared subsequently to vaccination and both ongoing local immune reaction and long-term persistence of $Al(OH)_3$ was observed	284
Al	Blood	AMS;-;-	Results of *in vitro* dissolution and *in vivo* absorption studies were reported indicating that Al-containing adjuvants administered intramuscularly are absorbed into the body	109
Al	Brain	AMS;-;-	The kinetics of Al distribution in brain and the effect of desferrioxamine were studied in rats using ^{26}Al as a tracer	36
Al	Total body	AMS;-;-	Features and applications of AMS to human nutrition were reviewed	35
Al	Biological fluids	-;-;-	This paper reviewed present knowledge on the intestinal absorption of Al in renal failure	119
As	Blood	AA;Hy;L	Blood As levels were investigated in humans in relation to plasma levels of reactive oxidants and antioxidant capacity	124
As	Urine	AA;Hy;L	160 spot urine samples and corresponding 24 h collections were measured for inorganic As, to determine appropriate sampling procedures. No differences were seen between the different sample types or whether creatinine was adjusted or not	3
As	Urine	AA;Hy;HPLC	Seafood consumption did not influence the levels of As^{III}, As^{V}, MMA, DMA or their ratios in urine	285
As	Urine	AF;Hy;HPLC	The effect of storage temperature (25, 4 and −20 °C) and storage duration (up to 5 months) on the stability of MMA^{III} and DMA^{III} in deionized water and human urine was studied using HPLC-HG-AFS for species detection	128
As	Urine, bile	AF;Hy;HPLC	As metabolism and speciation was studied in rats, mice, hamsters, rabbits, and guinea pigs injected with As^{V} or As^{III}	127
As	Urine	MS;ICP;HPLC	As metabolites were monitored over a 4-d period after ingestion of a synthetic arsenosugar, to investigate potential toxicity of marine algae used as human food	286
As	Urine	MS;ICP;HPLC	Increased excretion of penta- and uroporphyrins was demonstrated for workers exposed to As; As^{III} was the species best correlated with urinary porphyrin excretion	125
As	Bile, urine, tissue	MS;ICP;HPLC	As metabolic pathways were studied in rats by metabolic balance and speciation studies	287
As	Human milk	AA;Hy;L	As levels in human milk samples from different German areas were mostly below the LOD (0.3 μg l^{-1}). The highest concentration was 2.8 μg l^{-1}	126
As	Hair	AA;Hy;L	Hair As was determined by HGAAS after closed microwave digestion. Six digestion procedures were compared using recovery of inorganic and organic As compounds and the analysis of hair CRMs	123, 98
As	Hair	AA;Hy;-	Hair As levels in Egyptians ranged from 0.04 to 1.04 mg As kg^{-1} hair, with 45% of the samples exceeding the reference range (0.08 0.25 mg As kg^{-1} hair)	100
As	Chinese medicines	AA;ETA;L	Samples were digested under pressure with HNO_3 $HClO_4$ as oxidant. The chemical modifiers were $PdCl_2$ for As and $(NH_4)_2HPO_4$ for Pb. LODs were 3.75 ng ml^{-1} (As) and 1.8 ng ml^{-1} (Pb)	288
B	Blood, bone, urine	AA;ETA;-	Several elements were investigated as potential chemical modifiers in the determination of B in biological samples. The best results were obtained with the addition of Zr and citric acid onto Zr-coated platforms. LOD was 60 μg l^{-1} and m_0 = 282 pg.	130
B	Blood	AE;ICP;L	B was determined in blood by ICP-AES after protein removal with TCA. Precision was <5% and recoveries ranged from 95.6 to 96.2%. Results were compared with an ICP-MS direct method (r = 0.994). The method is one of the fastest for B determination in blood	15
B	Tissue	AE;DCP;L	B delivery to tissues, using folate receptor-targeted liposomes, was investigated	289

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Bi	Tissue	AA;ETA;L	Tissues were microwave digested with HNO_3 30% H_2O_2. Addition of Pt (2 μg) and 4% w/v tartaric acid (10 μl) was used as chemical modifier. The value of m_o was 22 pg and RSD% ranged from 1.4 to 4.8%	129
Ca	Urine, dialysate	AA;-;L	Ca, Mg and Zn were determined in urine and dialysate from subjects undergoing continuous renal replacement therapy. Results indicated loss of Ca and Mg, but not Zn	79
Ca	Urine	AE;ICP;L	The matrix effect, due to NaCl, KCl, $CaCO_3$, $MgCl_2$, $NH_4H_2PO_4$, HCl, H_2SO_4, urea and their concentration levels, was evaluated. Na and K could be determined without any sample preparation. For Ca and Mg, internal standardisation and a matrix-matching technique was necessary	290
Ca	Blood, faeces, milk, urine	AE;ICP;L	A balance study for Ca, Mg and P was carried out on 10 extremely low birthweight (< 1000 g) infants to assess nutritional needs	12
Ca	Urine	MS;ICP;L	A new method was reported for the determination of Ca isotope ratios and total Ca by means of a double focusing sector field ICP-MS equipped with a shielded torch. Factors influencing the uncertainty of the determination of Ca absorption were discussed	31
Ca	Bone	AA;F;L	The relationship of Ca and Sr concentrations in human bones to age and sex was investigated. Mineral content was lower in women and in older subjects	78
Ca	Arteries	AE;ICP;L	Ca, Fe and Mg were determined in rabbit arteries. Samples were acid digested in a closed-vessel microwave. The method is applicable to small clinical samples or arterial samples from very small animals	291
Ca	Total body	AMS;-;-	See Al, ref. 35	35
Cd	Serum	AA;ETA;L	Cd determination by ETAAS was used as the quantitative step of a new immunoassay method using EDTA Cd^{2+} chelate as a label. The LOD for α-fetoprotein was 0.12 ng ml^{-1}, CVs <8% and recoveries in the range 90–110%. Comparison with time-resolved fluoroimmunoassay gave a correlation coefficient of 0.993	92
Cd	Plasma	AA;ETA;L	For Cd and Pb analysis, plasma was dry-ashed and the inorganic residue dissolved in diluted high-purity HNO_3. Hg was determined directly. Ranges for Cd, Hg and Pb in cat plasma were 0.1–9, 0.3–15 and 1.2–50 μg l^{-1}, respectively	292
Cd	Blood	AA;ETA;L	Childhood exposure to Cd and Pb in the Ribeira river valley (Brazil) was investigated. Mean blood Pb level in children living close to a Pb refinery was 11.25 μg dl^{-1}	132
Cd	Blood	AA;ETA;L	Blood Cd was measured in 119 Turkish subjects, aged 17–77 years. Female smokers had the highest blood Cd (median: 0.90 ng ml^{-1} Cd)	293
Cd	Urine	AA;ETA;L	The assessment of a screening method for the determination of Cd, Ni and Pb in biological monitoring programmes was reported. Samples were pre-treated with acids, then digested *via* a microwave oven prior to analysis	294
Cd	Human milk, urine	AA;-;L	A significant positive correlation was found between maternal urinary Cd and Cd in breast milk. Maternal exposure to Cd seemed to increase early delivery, which led to a lower birth weight	134
Cd	Biological samples (CRMs)	AA;ETA;-	Three chemical modifiers were compared. A solution of 1% Triton X-100 0.2% HNO_3 was used as diluent. Zeeman background correction was applied. A mixture of Ni Pd $NH_4H_2PO_4$ gave the best performance. LODs were 0.04 and 0.92 μg l^{-1} for Cd and Pb, respectively	295
Cd	Hair	AA;ETA;Sl	Three media, 0.1% v/v Triton X-100, 0.14 mol l^{-1} HNO_3, and 0.1% v/v of CFA-C (a mixture of tertiary amines), for the preparation of hair slurries were compared. CFA-C gave the best results	99
Cd	Faeces	MS;ICP;-	Apparent fractional absorption of Cd from sunflower kernels was determined in women using sunflower kernels labelled with the stable isotope ^{113}Cd	296
Cd	Tissue (animal)	MS;ICP;CE	A method for the separation of metallothionein isoforms (MT) by CZE and UV or ICP-MS detection was developed. Analyses of mixtures of MT1 and MT2 from rabbit liver and mussel hepatopancreas cytosols (after exposure to metals) were reported	33
Cd	Brain	MS;ICP;-	Cd and Zn were determined in samples of brain tissue from subjects with Alzheimer's Disease (AD): subjects with senile involutive cortical changes and controls. No significant differences were observed for Cd, whereas Zn appeared to be lower in AD subjects	131
Cd	Tissues, urine	MS;ICP;-	*Post-mortem* samples of lung, liver, kidney and urine from 61 subjects were analysed for Cd, Cu and Zn. Results for Cd were presented	133
Cd	Kidney	XRF;-;-	Cd concentrations of 7 ppm were measured within 1 h in a rat kidney specimen using microbeam XRF and microbeam X-ray absorption measurements	297
Ce	Duodenal tissue	SIMS;-;-	The application of SIMS to studies of element microdistribution is illustrated with data from the determination of Ce or Th contamination of rat duodenal tissue, after ablation of specimens by ion bombardment	298

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Cr	Saliva, serum	AA;ETA;L	Concentrations of Cr and Ni in saliva and serum of 100 subjects with fixed orthodontic appliances did not provide evidence for potential toxicity	135
Cr	Blood cells	AA;ETA;L	Cr was determined in blood fractions of 86 blood donors and 35 type 2 diabetics	136
Cr	Urine	MS;ICP;L	Interferences from $^{40}Ar^{12}C^+$, $^{35}Cl^{16}OH^+$, $^{34}S^{18}O$, $^{40}Ar^{12}CH^+$ and $^{37}Cl^{16}O^+$ ions on ^{52}Cr and ^{53}Cr were reduced by approximately 2 3 orders of magnitude by using 1.0 ml min^{-1} NH_3 as reaction cell gas in the DRC and a q value of 0.6. LODs for ^{52}Cr and ^{53}Cr were 0.015 and 0.024 ng ml^{-1}, respectively	32
Cr	Reproductive glands	XRF;-;- PIXE;-;-	Cr was detected in testicular tissue sections from mice treated by intraperitoneal injection of 1 mmol kg^{-1} $CrCl_3$, with higher concentrations in the tunica albuginea and in isolated cells from the interstitial connective tissue	44
Cr	Medicinal herbs	XRF;-;-	Methodologies for the preconcentration and determination of Cr in medicinal herbs were compared	252
Cr	Water, gastrointestinal perfusate, serum	LEAFS;ETA;L	Laser radiation was used to excite Cr and fluorescence emission was observed at 302.2 nm or 357.9 nm. Atomisation of samples of water, gastrointestinal perfusate solutions and serum was performed in pyrolytically coated graphite tubes, using either 2.5 g l^{-1} $Mg(NO_3)_2$, 2% Triton X-100 or no modifier. LOD was 80 fg	89
Cu	Serum	AA;F;L	The determination of Cu and Zn in 100 µl of serum by derivative microsampling FAAS was reported	84
Cu	Serum	AA;F;L	Factors influencing Cu and Zn concentrations in serum of individuals from the Canary Islands were discussed	139
Cu	Serum	AA;ETA;L	Cu, Fe and Zn were determined simultaneously in serum diluted 80-fold with 0.01% w/v Triton X-100 1% v/v HNO_3	71
Cu	Seminal plasma	AA;ETA;-	Tungsten probes were used to introduce the sample into the graphite tube, providing better sensitivity and LOD	90
Cu	Aqueous humour	AA;ETA;L	Cu, but not Fe, in the aqueous humour of steroid-treated rabbits was significantly lower ($P < 0.001$) than in controls	299
Cu	Hair	AA;ETA;Sl	See Cd, ref. 99	99
Cu	Biological samples	AA;ETA;L AA;ETA;Sl	A W Rh treatment on the platform was used as a permanent modifier for the determination of Cu in digested and slurry samples. Results were comparable to those obtained with Pd + $Mg(NO_3)_2$, but the tube lifetime was increased and there was less variation of analytical slopes	138
Cu	Testicular tissue	AA;-;-	Growth retardation and altered levels of Cu, Fe and Zn in testicular tissue were observed in adult male rats exposed to formaldehyde	300
Cu	Liver	AA;F;S	A new device for the direct introduction of solid samples in FAAS is described using the determination of Cu in a Bovine Liver RM as an example	85
Cu	Human milk	XRF;-;-	Mean Cu, Fe and Zn concentrations measured in colostrum were: 0.54 ± 0.29 mg l^{-1}, 1.72 ± 1.01 mg l^{-1} and 6.97 ± 2.82 mg l^{-1}, respectively	60
Cu	Breast tissue	XRF;-;-	Cu, Fe and Zn levels were determined in 80 samples of healthy tissue or breast carcinomas. Higher levels Cu, Fe and Zn were observed in tumour tissue	39
Eu	Serum	MS;ICP;L	Eu^{3+}-labelled streptavidin was used as part of an immunoreaction system. The concentration of thyroid stimulating hormone in serum was determined by measuring the Eu^{3+} fraction bound to the immunocomplex	91
Fe	Serum	AA;ETA;L	See Cu, ref. 71	71
Fe	Arteries	AE;ICP;L	See Ca, ref. 291	291
Fe	Aqueous humour	AA;ETA;L	See Cu, ref. 299	299
Fe	Testicular tissue	AA;-;-	See Cu, ref. 300	300
Fe	Human milk	XRF;-;-	See Cu, ref. 60	60
Fe	Bone	XRF;-;-	Fe was found in significant quantities in the lagenal otoliths of birds. This comprised tiny magnetic particles which may provide a geomagnetic sensory input, from which navigational information could be inferred	68
Fe	Breast tissue	XRF;-;-	See Cu, ref. 39	39
Gd	Urine	AE;ICP;FI	Gd^{III} was complexed with 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol in the presence of non-ionic micelles of PONPE-7.5. The micellar system was loaded into the FIA, where the surfactant rich-phase was retained in a micro-column and later eluted with 4 mol l^{-1} HNO_3 directly into the plasma. The enhancement factor was 20 for a 10 ml sample. LOD was 40 ng l^{-1}	6
Hg	Blood	AA;CV;L	In a study of 106 urban elderly subjects, no relation was observed between blood Hg and cognitive function, arterial blood pressure, age, gender or body mass index	301

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Hg	Blood, urine	AA;CV;L	Samples were acid-digested in closed vessels with a HNO_3 $HClO_4$ mixture in a microwave oven. Hg complexes with *O,O*-diethyldithiophosphoric acid ammonium salt were retained on a C_{18} column and eluted with CH_3OH. After on-line reduction with $NaBH_4$, Hg was measured. LOD was 20 ng l^{-1}	151
Hg	Blood, urine, saliva	AA;CV;L	Hg levels in blood and urine of subjects with amalgam fillings were not different between those claiming or not claiming symptoms. Hg levels in saliva did not correlate with the concentrations in blood and urine	159
Hg	Plasma	AA;ETA;L	See Cd, ref. 292	292
Hg	Urine	AA;Hy;L MS;ICP;FI	Reference values for Hg in urine obtained from 383 subjects from 4 Italian cities were reported. The median was 0.8 μg g^{-1} creatinine	160
Hg	Urine	MS;CV;FI AA;CV;FI	Total Hg was determined after on-line oxidative treatment of the sample in a microwave oven, using a KBr $KBrO_3$ mixture and final oxidation with $KMnO_4$. LOD was 0.03 μg l^{-1} Hg and precision less than 2 3%, compared with 0.2 μg l^{-1} and 3 5% for AAS detection	152
Hg	Hair, Chinese medicines (CRM)	AA;CV;L	Hg was determined by CVAAS after sample pressure dissociation with a mixture of HNO_3 H_2SO_4 H_2O_2 (4 + 1 + 1) and $SnCl_2$ as the reducing agent. Air could be used instead of Ar as the carrier gas. LOD was 0.5 ng ml^{-1}, RSD was <3.2% and recovery was 94.6 102%	153
Hg	Hair	AA;ETA;L	Hg was determined after acid digestion and complexation with 2,3-dimercaptopropane-1-sulfonate. Methylmercury was extracted from hair with 2.0 M HCl and analysed directly	101
Hg	Hair	AF;CV;GC	Methylmercury was measured in human hair after acid digestion using aqueous ethylation and headspace solid-phase microextraction sampling. LODs for methylmercury and Hg^{2+} were 50 and 80 ng g^{-1}, respectively, for 100 mg of human hair	102
Hg	Hair	MS;ICP;HPLC	To separate inorganic and methylmercury, 0.1 g hair samples were cold digested with 2 ml HNO_3 1 ml H_2O_2. 0.1 M HCl was efficient for the removal of methylmercury, but removed only 65% of the spiked inorganic Hg	96
Hg	Chinese medicines	AA;-;S AA;CV;- MS;ICP;-	Hg was determined in Chinese medicines using AA coupled with a pyrolysis unit. This arrangement allowed the analysis of solid samples (20 mg) without any sample pretreatment. Precision on real samples was 3 7% and recovery was 97.6 102.7%. The method compared well with CVAAS and ICP-MS	105
Hg	Placenta	AF;CV;L	Both inorganic Hg and methylmercury were determined in placentas from 119 Swedish women. Inorganic Hg increased with the number of dental fillings	158
Hg	Biological samples	AF;CV;HPLC	A method was developed for the separation and determination of methylmercury in biological samples after a microwave-assisted alkaline digestion. LOD was 10 μg kg^{-1} and RSD <8% for concentrations ranging from 0.15 to 3.0 mg kg^{-1}	157
Hg	Biological samples	AE;MIP;GC	Sample preparation involved microwave extraction with 3 M HCl, followed by aqueous-phase derivatisation with sodium tetraphenylborate and solid phase microextraction with a silica fibre coated with polydimethylsiloxane	154
Hg	Biological materials	MS;ICP;ETV	No sample preparation was required. The solid sample was inserted into a graphite furnace of the boat-in-tube type. Speciation was achieved by selective temperature programming. ID was used for quantification	150
K	Urine	AE;ICP;L	See Ca ref. 290	290
Mg	Urine, dialysate	AA;-;-	See Ca, ref. 79	79
Mg	Blood, faeces, milk, urine	AE;ICP;L	See Ca, ref. 12	12
Mg	Urine	AE;ICP;L	See Ca ref. 290	290
Mg	Arteries	AE;ICP;L	See Ca, ref. 291	291
Mn	Serum	AA;ETA;L	Serum Mn levels were determined in 250 healthy subjects aged 15 90 years. The geometric mean was 1.1 μg l^{-1}, range: 0.3 2.5 μg l^{-1}. Results were studied in relation to age and gender	149
Mn	Serum	AA;ETA;L	Samples were diluted 1 + 3 with 1.0% v/v HNO_3 0.10% w/v Triton X-100. The chemical modifier was Pd (20 μg) + $Mg(NO_3)_2$ (10 μg). An oxidant mixture (15% w/w H_2O_2 + 1.0% v/v HNO_3) was added to reduce carbon build-up. The values of m_o were 6 pg (Mn) and 46 pg (Se). LODs were 6.5 pg (Mn) and 50 pg (Se)	70
Mn	Herbal medicines	AA;ETA;Sl	A 10% glycerol solution was used as the slurry medium and chemical modifier in a molybdenum atomiser tube. The LOD was 69 fg. Results were in agreement with those obtained on acid-digested samples	107
Mo	Blood	AA;ETA;L	Samples were diluted 1 + 2 with 0.1% v/v Triton X-100. Hb (25 μg) was used as a chemical modifier. Build up of carbonaceous residues was reduced by a 'blank' analysis of 20 μl 15% w/v H_2O_2 every 5 firings. LOD was 0.6 μg l^{-1} and m_o 7.2 pg	164
Mo	Urine	AA;-;-	Procedures for the collection of urine for Mo analysis in children were evaluated. Mo concentrations in 24 h specimens ranged from 0 to 124 μg l^{-1}	162

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Mo	Urine	MS;ICP;L	Samples were diluted with 1% HNO_3 (v/v). In and Y were used as internal standards. Determinations were carried out at ^{98}Mo. LOD was 0.2 $\mu g\ l^{-1}$	161
Mo	Faeces, plasma	AA;-;- MS;ICP;-	Balance studies were carried out to investigate Mo deficiency in infants with preternatural anus	302
Mo	Faeces, urine	AA;-;- MS;ICP;-	Mo absorption and kinetics of excretion was investigated in 10 infants with a gestational age of 35 (30 39) weeks, using ^{100}Mo as an extrinsic tag	163
Na	Urine	AE;ICP;L	See Ca, ref. 290	290
Ni	Saliva, serum	AA;ETA;-	See Cr, ref. 135	135
Ni	Serum, urine	AA;ETA;L	A method using aqueous calibration standards and H_2O_2 as a chemical modifier was proposed. LOD was 0.2 $\mu g\ l^{-1}$ for both serum and urine samples. RSD was 10 15% for serum samples and 8 10% for urine samples, at concentrations of 0.5 2.5 $\mu g\ l^{-1}$	165
Ni	Urine	AA;ETA;L	See Cd, ref. 294	294
Ni	Urine, drinking water, industrial waste water	AA;F;L	Ni was retained on Diaion HP-20 resin as 1-nitroso-2-naphthol complex and eluted with 1 M HNO_3 in acetone, prior to FAAS determination	166
Ni	Skin	AE;ICP;- MS;ICP;-	Skin adsorption and penetration of Ni salts was investigated *in vivo*	167,168, 169
Ni	Tissue	MS;ICP;LA	Spatial distribution around Ni-containing implants was assessed *in vivo* in rats	170
P	Blood, faeces, milk, urine	AE;ICP;L	See Ca, ref 12	12
Pb	Blood, urine	AA;ETA;L MS;ICP;L	The performances of specialised laboratories using ETAAS, ASV or ICP-MS techniques to determine Pb in blood or urine were compared	94
Pb	Blood, urine	AA;ETA;L	Ir was used as a thermally deposited permanent modifier in the determination of Pb in blood and urine, diluted with a mixture of 0.1% Triton X-100 0.2% HNO_3. Results were comparable to those obtained with a conventional phosphate modifier. The Ir coating increased tube lifetime up to 1100 cycles	141
Pb	Blood	AA;ETA;L	To investigate Pb exposure and renal tubular damage among adolescent workers in auto repair workshops in Turkey, blood Pb and urinary *N*-acetyl β-D-glucosaminidase activity were measured in 39 adolescent workers. Both parameters were higher than in the control groups	145
Pb	Blood	AA;ETA;L	See Cd, ref. 132	132
Pb	Plasma	AA;ETA;L	See Cd, ref. 292	292
Pb	Blood, urine	AA;ETA;L	Rh was investigated as a permanent modifier for the atomization of Pb from biological fluids in tungsten filament AAS. The Rh coating greatly improved the filament lifetime and allowed calibration with aqueous Pb standards	87
Pb	Blood	AA;ETA;L	The performances of the portable LeadCare Blood Lead Testing System were assessed by comparison with ETAAS	142
Pb	Blood, plasma	MS;ICP;L	In a longitudinal study, whole blood and plasma samples from 63 women were analysed for Pb by using HR-ICP-MS. Plasma Pb was associated with blood Pb and may be applied to general clinical settings, provided that appropriate sampling techniques are adopted	146
Pb	Urine	AA;ETA;L	See Cd, ref. 294	294
Pb	Tissue	AA;-;-	No increase of gastrointestinal Pb absorption was observed in rats undergoing oral treatment with the chelating agent *meso*-2,3-dimercaptosuccinic acid	303
Pb	Brain	AA;ETA;L	Pb concentrations were determined in brain tissue from cases and controls to investigate Pb role in the development of diffuse neurofibrillary tangles with calcification	143
Pb	Biological samples (CRMs)	AA;ETA;L	See Cd, ref. 295	295
Pb	Hair	AA;ETA;Sl	See Cd, ref. 99	99
Pb	Teeth	AA;ETA;L	Mean Pb in teeth from First Nation schoolchildren (Canada) was 9.2 $\mu g\ g^{-1}$ dry weight. Consumption of contaminated game meat is suggested as a possible source of exposure	147
Pb	Teeth	AA;ETA;L	To evaluate Pb exposure in children, Pb was measured in 309 shed primary teeth collected from children (aged 7.6 ± 1.2 years) in Karachi. Mean Pb level was 5.78 $\mu g\ g^{-1}$ dry weight, range: 0.42 39.75 $\mu g\ g^{-1}$	77
Pb	Bone	AA;ETA;L	Low Pb concentrations in bone were determined in samples digested in a pressurized microwave system with 70% HNO_3. The use of $Mg(NO_3)_2$ Pd as a chemical modifier avoided the spectral interferences arising from addition of $NH_4H_2PO_4$ to Ca rich matrices. LOD was 0.06 $\mu g\ g^{-1}$ dry mass. NIST SRM 1486 was used for validation	304
Pb	Chinese medicines	AA;ETA;L	See As, ref. 288	288
Pb	Biological and geological samples	MS;ICP;HG	The determination of Pb by HG-ICP-MS yielded an improved LOD of 0.002 ng ml^{-1}, compared with ICP-MS and HG-AFS. The performances of single- and double-stage gas liquid separators were investigated	305

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Pb	Bone, blood, urine	XRF;-;S AA;ETA;L MS;ICP;L	In an epidemiological study of middle-aged and elderly men, the relation between bone, blood and urine Pb levels suggested that bone resorption influences the release of bone Pb stores into the circulation	55
Pb	Bone	XRF;-;-	An association between bone Pb concentration and blood pressure in early adult life was observed in persons exposed to Pb during childhood	52
Pb	Bone, blood	XRF;-;-	Bone Pb levels were higher in retired blue collar workers compared to other occupations. The effect was markedly stronger in non-white blue collar workers	54
Pb	Bone, blood	XRF;-;- AA;ETA;L	In a study of 264 women aged 46–74 years, use of postmenopausal oestrogen (inverse) and alcohol intake (positive) were significantly associated with blood Pb levels. Both bone Pb measures were significantly and positively associated with blood Pb but only among postmenopausal women not using oestrogen	56
Pb	Bone, blood	XRF;-;- AA;ETA;L	Measurements of Pb in blood during breastfeeding, corrected for maternal bone Pb, supported the hypothesis that lactation stimulates Pb release from bone to blood	53
Pb	Bone, blood	AA;ETA;L XRF;-;-	Pb levels in cord blood and maternal trabecular bone were significantly, independently, and inversely associated with the Mental Development Index scores of the Bayley Scale	148
Pb	Blood, bone	XRF;-;- AA;ETA;L	In a case-control study, using both biochemical measures (blood and bone Pb) and interviews, the risk of amyotrophic lateral sclerosis (ALS) was associated with higher blood and bone Pb levels. These results are consistent with a potential role for Pb exposure in the etiology of ALS	306
Pb	Bone	XRF;-;S AA;ETA;L	The accuracy of XRF determination in pig bones was investigated by comparison with ETAAS measurements	307
Pb	Bone	XRF;-;-	These papers review theoretical considerations relevant to the application of L-shell XRF for *in vivo* measurement of Pb in bone and report on the development of an L-shell XRF system	45,46,51
Pb	Bone	XRF;-;S	A correction for the calculation of Pb concentrations and their uncertainties was proposed	47
Pb	Bone	AA;ETA;L XRF;-;-	Pb concentration in tibia surface was greater than in core. XRF measurements agreed with ETAAS for tibia surface but overestimated Pb concentrations for core tibia	49,50
Pd	Urine	AA;ETA;L	The Pd DDC complex was retained on a column of silica C_{18} and eluted with 43 μL of ethanol directly into the graphite furnace. LOD was 9 ng l^{-1} and RSD between 11.3 and 4.8%	7
Pt	Clinical samples	AA;-;- AE;-;- MS;ICP;L ASV;-;-	The paper reviews techniques for the determination of Pt in clinical samples, including preconcentration and speciation methods	171
Pt	Plasma	AA;ETA;HPLC	A method was developed to determine simultaneously cisplatin and its hydrolysis product monohydrated cisplatin in plasma	174
Pt	Plasma	AA;ETA;L	Samples were diluted 1 + 4 with 0.2 mol l^{-1} HCl. LOQ was 0.25 μmol l^{-1}. RSD% was less than 14%	173
Pt	Plasma	AA;ETA;L	Total Pt, oxaliplatin and Pt(dach)Cl^{2-} were measured in plasma ultrafiltrate of patients undergoing oxaliplatin administration in order to assess the relation between oxaliplatin biotransformation and toxicity	308
Pt	Plasma, urine	AA;-;-	The concentrations of free Pt in plasma and urine of 12 children receiving cisplatin were measured in relation to the risk of nephrotoxicity	309
Pt	Blood cells	MS;ICP;HPLC	The concentrations of satraplatin and Pt-containing products in whole blood and other biological fluids were measured to investigate the *in vitro* biotransformation of satraplatin, a candidate anticancer drug	176
Pt	Tissues	AA;-;-	The *in vitro* scleral permeability of carboplatin using different vehicles was compared *in vitro* and *in vivo*	310
Pt	Tissue	AA;ETA;L	Pt was measured in blood and tissues (placenta and maternal and foetal kidney; liver, brain, lung, heart, muscle) of pregnant rats, given intravenous cisplatin or an alternative cytostatic drug, Bamet-R2. Cisplatin showed higher accumulation in foetal tissues, mainly kidney, lung and heart	175
Pt	Tissue	XRF;-;-	Pt from cisplatin was determined in biopsy tissues and blood serum samples from patients with advanced bladder cancers. LOD was 0.01 ppm and LOQ 0.1 ppm	67
REEs	Urine	MS;ICP;ETV	Urine was injected directly into the graphite tube. Trifluoromethane (Freon-23) was used as a chemical modifier. LODs were in the range 1–10 ng l^{-1}. The RSD was less than 10–15% at 100 ng l^{-1}	177
Sb	Liver, blood	AA;Hy;FI	Sb speciation was achieved by sequential on-line extraction with 1.5 mol l^{-1} acetic acid and 0.5 mol l^{-1} H_2SO_4 for Sb^{III} and Sb^{V}, respectively. Sb^{V} was then reduced on-line to Sb^{III} with *L*-cysteine prior to HG. LODs were 1.0 μg l^{-1} for Sb^{III} and 0.5 μg l^{-1} for Sb^{V}. Precision was 2%	121

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Sb	Blood, plasma, urine, hair	MS;ICP;L	Sb levels in whole blood, plasma, urine, and hair were monitored in patients with leishmaniasis before, during, and after administration of *N*-methylmeglumine antimonate. Speciation of Sb^{V} and Sb^{III} was performed by ion chromatography using EDTA (2 or 20 mM, pH 4.7) as the mobile phase	122
Se	Blood	AA;ETA;L	The method applied a Rh W coating to the integrated platform and a $RhCl_3$ solution as chemical modifier. Samples were diluted 1 + 4 v/v with 0.2% v/v HNO_3 0.5% v/v Triton X-100. The pyrolysis temperature could be increased to 1300 °C	178
Se	Plasma	AA;-;L	In a cross-sectional study of 103 older New Zealand women, suboptimal plasma Se and Zn levels were reported	80
Se	Serum, urine, hair	AA;ETA;L AA;Hy;L	Se was determined in biological samples using Rh as a chemical modifier. LOD was 6 ng ml^{-1}. Results for urine were compared with a FI-HG-ETAAS procedure and with HG-AFS. Two digestion procedures were described	179
Se	Plasma	AA;ETA;L	Plasma Se concentrations were measured 3.83 ± 1.85 y (mean ± SD) before the diagnosis of prostate cancer in cases and controls from the Baltimore Longitudinal Study of Aging Registry. Higher plasma Se levels were associated with a lower risk of cancer	184
Se	Serum, ascitic fluid	AA;ETA;L	Serum Se was lower in cirrhotic patients than in controls. Se levels in ascitic fluid were not different among the groups of patients examined	311
Se	Serum	AA;ETA;L	Age-related reference values for serum Se concentrations in infants and children were derived from 1010 children, aged 1 d to 15 y	181
Se	Serum	AA;ETA;L	See Mn, ref. 70	70
Se	Serum	AA;Hy;L	In patients with liver damage, serum Se was significantly lower than in controls. Cirrhotic patients had lower Se levels than subjects with hepatitis. Serum Se was correlated with cholesterol levels and inversely correlated with γ-glutamic-transferase activities	312
Se	Blood, urine	AA;Hy;L	This study investigated changes of Se levels in relation to the presence of amalgam dental fillings	74,75
Se	Plasma, hair	AA;Hy;L	Measurements of Se in plasma and hair of a sample of the general population in Poland suggest the need for Se supplementation in the diet	313
Se	Serum	AF;Hy;L	Serum Se levels were not different between pregnant women with or without gestational diabetes mellitus	183
Se	Serum	AE;ICP;L	The capabilities of a high-resolution spectrometer with laterally viewed ICP for Se determination in serum were investigated. Samples were pressure digested with HNO_3. LOD was 0.01 0.02 mg l^{-1}	180
Se	Blood, hair	MS;ICP;-	Blood and hair Se concentrations were measured in 26 women with a history of recurrent miscarriage and 18 controls. No significant difference was observed between blood Se levels but the control group had significantly higher concentrations (0.14 μg g^{-1} *versus* 0.34 μg g^{-1}) of Se in hair	182
Se	Serum	XRF;-;-	Serum Se concentrations from 10 to 66 ng ml^{-1} were determined in 78 suckling 2-month-old calves	62
Se	Urine	AF;Hy;L	The stability of Se in urine with time and storage temperature is reported. HCl was not effective as a preservative	5
Se	Urine	MS;ICP;IPC	Se species were separated by ion-pairing chromatography with ICP-MS detection. Heptafluorobutanoic acid and nonafluoropentanoic acid were used as ion-pairing agents. The method was used to investigate Se species in urine	314
Se	Urine	MS;ICP;HPLC	Se^{VI}, selenourea , selenomethionine , selenoethionine, and trimethylselenonium ion were separated by reverse phase HPLC using a solution of 2.5 mM Na 1-butanesulfonate and 8 mM TMAH as ion-pair reagent. Urine was injected directly onto the column. LODs ranged from 0.6 to 1.5 ng Se ml^{-1}. Two unknown Se species were detected in urine	315
Se	Urine	MS;ICP;HPLC MS;ESI;-	The major Se metabolite in rat urine was identified as Se-methyl-*N*-acetylselenohexosamine	316
Se	Brain	AA;ETA;L	Microwaved digested samples of human brain were analysed without dilution. Pd (Se) and W (Sn) were used as chemical modifiers. Se in brain ranged from 200 to 700 ng g^{-1} and Sn from 20 to 300 ng g^{-1} dry weight	73
Se	Liver	AF;Hy;L	The speciation and subcellular location of Se-containing proteins in human liver was investigated	317
Se	Proteins	MS;ICP;ETV	Proteins were fractionated by means of SDS-PAGE and Se determined in the gel bands	318
Si	Biological and clinical samples	MS;ICP;-	A method was developed, based on ID and HR-ICP-MS. Samples were microwave digested with either HNO_3 or a mixture of HNO_3 and HF. Blank control required water purification and special equipment, such as a PFA nebuliser and spray chamber, sapphire injection tube and a silicon nitride torch	185
Sn	Brain	AA;ETA;-	See Se, ref. 73	73
Sr	Bone	AA;F;L	See Ca, ref. 78	78

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Te	Urine	AA;Hy;L	A new method for the determination of Te in urine by HG AAS with derivative signal processing was developed. Both LOD (0.26 μg l^{-1}) and the characteristic concentration (0.042 μg l^{-1}) were reported to be better than those of conventional HG AAS	187
Th	Urine	MS;ICP;L	The performance of methods for the determination of ^{232}Th, ^{235}U and ^{238}U, based on quadrupole or magnetic sector ICP-MS, were compared	27
Th	Duodenal tissue	SIMS;-;-	See Ce, ref. 298	298
Ti	Blood	AE;ICP;L	TiO_2 was administered to male volunteers, aged 24 to 66 y. Basal blood Ti concentrations, measured by ICP-AES after destruction of the organic matrix, were 11.2 μg l^{-1} (RSD 4.1%). Ti absorption from the gastrointestinal tract depended on the particle size. A high individual variability was observed for blood Ti concentrations in relation to the amount of Ti administered and time after dosage	188
Tl	Hair	MS;ICP;ETV	A method for the direct determination of the longitudinal distribution of Tl in human scalp hair was developed. LOD was 0.7 pg, corresponding to about 5 ng g^{-1} of dried hair	97
U	Urine	MS;ICP;L	A method was developed for the determination of U in urine by isotope dilution with ^{233}U. The procedure was validated by comparison with alpha-spectrometry and analysis of a CRM	189
U	Urine	MS;ICP;-	See Th, ref. 27	27
U	Urine, hair	MS;ICP;L INAA;-;-	U in urine samples from 103 Canadian Forces personnel was determined independently by two different methods: median concentrations were 2.8 ng l^{-1} (ICP-MS) and 15 ng l^{-1} (INAA). Isotope analysis, carried out on hair samples, did not show evidence of contamination with depleted U	190
U	Urine	XRF;-;-	U was determined in urine following a preconcentration step	61
V	Blood	AA;-;L	V pharmacokinetics and oral bioavailability was determined in rats administered vanadyl sulfate	191
V	Proteins	AA;ETA;L	The binding of V to human serum albumin, fresh frozen plasma and transferrin was investigated	192
V	Tissue	AA;-;-	V was determined in tissues of mice exposed intravaginally to vanadocene dithiocarbamate, an experimental contraceptive agent. V content in tissue (<1 μg g^{-1}) and other experimental evidence indicated lack of systemic toxicity or effects on reproductive performance after the experiment	193,319
Zn	Serum	AA;F;L	See Cu, ref. 84	84
Zn	Serum	AA;ETA;L	See Cu, ref. 71	71
Zn	Serum	AA;F;L	See Cu, ref. 139	139
Zn	Plasma	AA;-;L	See Se, ref. 80	80
Zn	Urine, dialysate	AA;-;-	See Ca, ref. 79	79
Zn	Urine	MS;ICP;L	Fractional Zn absorption in breast feeding women given Fe supplements was calculated using Zn stable isotopes and measuring Zn isotopic enrichments in urine	320
Zn	Human milk	XRF;-;-	See Cu, ref. 60	60
Zn	Proteins	MS;-;-	Nanospray and collisionally induced dissociation on a quadrupole/TOF mass spectrometer were used to investigate Zn complexes with proteins and peptides	321
Zn	Testicular tissue	AA;-;-	See Cu, ref. 300	300
Zn	Brain	MS;ICP;-	See Cd, ref. 131	131
Zn	Tissue	AE;ICP;L	The inhibition of bacterial growth in the rat prostate with chronic prostatitis after intraprostatic injection of Zn was investigated. Prostatic Zn levels were compared in treated rats and controls	322
Zn	Tissue	XRF;-;-	Differences were observed in Zn levels in cancerous and normal tissues of human prostate	40
Zn	Breast tissue	XRF;-;-	See Cu, ref. 39	39
Various	Biological and clinical samples, foods and beverages	-;-;-	The 2002 ASU highlighted recent trends, including work to validate the use of XRF, further applications of techniques for As speciation, and for the first time investigations involving organically produced foods	1
Various	Biological samples	-;-;-	Recent developments in metal speciation techniques were reviewed	2
Various (70)	Leachates	MS;ICP;L	Devices for sampling and storage of blood and serum were assessed for elemental contamination	4
Various (5)	Serum	AA;ETA;L	Cu, Mg, Mn, Pb and Zn were measured in surgical patients receiving total parenteral nutrition. Supplementation with essential elements is recommended	323
Various (7)	Erythrocytes, plasma	AA;ETA;L	The binding of Co, Cr, Cu, Fe, Mn, Ni and Zn to proteins in blood fractions was investigated by means of hydrophobic interaction chromatography and off-line ETAAS	81
Various (12)	Serum	AE;ICP;L	Al, Cd, Co, Cu, Fe, Mg, Mn, Mo, P, Pb, S, and Zn were determined in serum, its ultrafiltrates and hair of liquidators of the Chernobyl Nuclear Power Plant accident who were working in the disaster region in 1986 1987	324

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various (12)	Serum	MS;ICP;L	Al, Cd, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, Sr and Zn were determined in serum from 19 healthy subjects after digestion in a closed-vessel microwave oven with HNO_3 H_2O_2. For Al analysis, serum was digested at atmospheric pressure with TMAH	23
Various (14)	Serum	MS;ICP;L	Al, Cd, Ca, Co, Cr, Cu, Fe, Mn, Mo, Pb, Rb, Sr, U and Zn were determined in 1 + 4 diluted serum of 59 blood donors and 14 hemodialysed patients. Sc, Ga, Y and Ti were used as internal standards. Fe, Cu and Zn were also determined by isotope dilution analysis	29
Various (13)	Blood, serum	MS;ICP;L	Concentrations of Cd, Co, Cu, Hg, Pb, Rb, Rh, Pd, Pt, Se, Ti, W and Zn were determined in samples from 372 15-year-old adolescents in Sweden	22
Various (4)	Serum	XRF;-;L	Fe, Cu, Zn and Se were determined in serum samples from normal individuals and cancer patients	58
Various (4)	Serum	XRF;-;L	The applicability of direct TXRF to the determination of Br, Cu, Se and Zn in serum was investigated	57
Various (4)	Urine	AA;-;-	Cr, Cu, Ni and Pb were determined in urine after preconcentration on Amberlite XAD-2000 as 1-(2-pyridylazo)-2-naphthol chelates	325
Various (6)	Urine	MS;ICP; HG,GC	22 organic species of As, Ge, Hg, Sb, Se and Sn were detected and 18 identified in human urine after fish consumption. LODs ranged between 2 and 12 pg l^{-1}	30
Various (noble metals)	Urine	MS;ICP;ETV	A chelating agent, *O,O*-diethyldithiophosphate, and a non-ionic surfactant, Triton X-114, were added to acid-digested samples. At temperatures up to the cloud point, a surfactant-rich phase is separated, containing most of the noble metals complexed	172
Various (5)	Saliva	AE;ICP;L	Cd, Cu, Mn, Ni and Pb were preconcentrated on AGSOW-X8 resin and eluted with 3 mol l^{-1} HCl, using an on-line micro-scale flow system	14
Various (4)	Human milk	AA;-;L	The changes in Cd, Cu, Se and Zn content of Finnish human milk since Se supplementation of all agricultural fertilizers were documented	269
Various (23)	Bile, gallstone	AE;ICP;L	Samples were digested with HNO_3 (5 ml) and H_2O_2 (3 ml) in PTFE vessels. The concentrations of Al, As, B, Ba, Ca, Cd, Co, Cr, Cu, Fe, Hg, K, Li, Mg, Mn, Mo, Na, Ni, P, S, Ti, V and Zn were determined	17
Various (20)	Gastric juices	MS;ICP;-	Toxic elements (Al, Ba, Cd, Cr, Cu, Fe, Hg, Li, Mg, Mn, Ni, Pb, Sb, Sn, Sr, Te, Tl, V, W, Zn) were quickly released from button batteries in simulated gastric juice	25
Various (9)	Amniotic fluid, placenta	XRF;-;-	The elemental composition of amniotic fluid and samples was determined by TXRF after removal of the organic matrix with HNO_3 and O_2 plasma ashing. Placenta samples were lyophilised prior to analysis by EDXRF. Cr, Mn, Ni, Pb, Se and Sr concentrations were very low. Ca, Cu and Fe concentrations were correlated with mother's age and newborn weight	59
Various	Proteins	MS;ICP;L	The paper reported simultaneous determination of proteins using an element-tagged immunoassay coupled with ICP-MS detection	93
Various (7)	Brain	AE;ICP;L	Cu and other trace elements (Ca, Fe, Mg, P, S, Zn) were measured in the brain of a patient who died with Wilson's disease. Cu levels (88 158 μg g^{-1} dry weight) were higher than reference values	18
Various (16)	Tissue	AE;ICP;-	Al, As, Cd, Cr, Cu, Fe, Pb, Mn, Hg, Mo, Ni, Se, Si, Sn, V and Zn were measured in liver, kidney, cerebrum, heart, spleen, lung, bone, hair and nail from autopsied Koreans, aged 12 87 years	21,326
Various (14)	Tissue	AE;ICP;L	Autopsy tissue samples from the brain front lobe, cerebellum, heart, kidney (cortex and medulla), liver, pancreas, spleen and ovary were analysed for Al, B, Ba, Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb, Se, Sr and Zn in 30 (17 women and 13 men) subjects aged 17 96 y	19,20
Various (7)	Biological samples	AE;ICP;ETV,Sl	The direct analysis of micro-amounts of biological samples was reported. LODs for Ca, Cr, Cu, Fe, Ti, Y and Zn were 11.0, 2.0, 1.2, 2.5, 1.0, 5.8, and 242 ng ml^{-1}, respectively. RSDs ranged from 2.1% (Ti) to 4.4% (Cr)	16
Various (12)	Tissue	MS;ICP;-	Concentrations of As, Cd, Co, Cr, Cu, Pb, Mn, Hg, Ni, Sn, V and Zn in liver, lung, kidney, brain and bone samples from 78 non-occupationally exposed subjects were reported	24
Various	Tissue	MS;ICP;LA	Direct analysis of trace elements in thin sections of soft tissues was achieved using a cryogenically cooled ablation cell. Precision of 2 6% was achieved for tissue samples ablated at temperatures below −60 °C	34
Various (5)	Lung, soil (CRMs)	MS;ICP;-	High-performance chelation IC coupled to SF-ICP-MS was used to separate and determine Am, Np, Pu, Th and U. The method was tested on CRMs (NIST 4251 Human Lung and 4353 Rocky Flats Soil)	28
Various (5)	Tissues	XRF;-;-	Concentrations of at least 5 elements (As, Cu, Fe, Pb and Zn) were determined in *post mortem* soft tissues from a Portuguese king to clarify the circumstances of his death in 1826	327

Table 1 Analysis of clinical and biological materials (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various (14)	Tissue	XRF;-;-	Various elements (As, Br, Ca, Co, Cu, Fe, K, Mn, Ni, P, Rb, Se, Sr, Zn) were determined in *post-mortem* samples of liver, brain and kidney from subjects suffering from liver cirrhosis and controls. Increased amounts of Zn were found in kidneys from subjects with cirrhosis	64
Various (9)	Tissue	PIXE;-;-	Elemental distributions at the tracheal and bronchial mucosas were chemically characterised. Al, Cr, Cu, Fe, Ni, Si, Ti, V and Zn were detected at the distal respiratory tract. Al, Si, Ti, Fe and Cr accumulated mostly in the phagocytic cells and capsule of lymph nodes, while V and Ni accumulated in the cortex and paracortex medullar areas	43
Various (15)	Tissue (dolphin)	XRF;-;-	The concentrations of As, Br, Ca, Co, Cu, Fe, Hg, K, Mn, Ni, Pb, Rb, Se, Sr and Zn, were measured in muscle, liver, fat tissue and skin of two dolphin species. Differences were observed between tissue types	110
Various (6)	Teeth	AA;F;L AA;ETA;-	Ca, Cu, Mg, Pb, Sr and Zn were determined in 67 deciduous teeth from children in Venezuela, aged 87.76 ± 34.50 months, range 29 151 months	76
Various (18)	Mane hair (horse)	AE;ICP;-	The concentrations of As, Al, Ca, Cd, Cr, Cu, Fe, Hg, K, Mg, Mn, Na, Ni, P, Pb, Se, Si and Zn in the mane hair of racing horses were determined	104
Various (7)	Hair	MS;ICP;L	Methods for the pre-treatment and determination of As, Cd, Cr, Hg, Pb, Sb and Se in human hair were developed. Washing with 0.1 M HCl was efficient for the removal of external Cd, Hg and Pb, whereas, for As, Cr and Sb, 1 % (v/v) sodium lauryl sulfate was preferred. Se was not removed from the hair by any of the washing methods studied	95
Various (4)	Chinese medicinal material	MS;ICP;Hy	A novel sample introduction technique was applied to the determination of As, Se, Ge, and Hg by either the Hy or CV technique coupled with ICP-MS detection. Only 4 μL of sample were required for CV generation. LODs were in the fg range	106

[a]Hy indicates hydride and S, L, G and Sl signify solid, liquid, gas or slurry introduction, respectively. Other abbreviations are listed elsewhere.

1.9.23 Titanium. Bockmann *et al.*[188] used ICP-AES to determine levels of Ti in blood before and after oral administration of TiO_2 to human volunteers. Pre-treatment of the blood sample, to remove the organic matrix, was necessary to obtain accurate results. The authors reported *a 'normal' blood Ti concentration of 11.2 μg l^{-1}*. They observed that absorption from the gastro-intestinal tract of Ti administered, in capsules or as a powder, was influenced by mean particle size. They hypothesised that poorer absorption of larger diameter particles was due to agglomeration.

1.9.24 Uranium and actinides. Following concerns over the potential exposure of military personnel to U during service in the Gulf war and Kosovo, there has been increased activity in the measurement of actinides in environmental and biological samples. *A number of groups have reported methods for the determination of U in biological matrices.* Pappas *et al.*[27] investigated optimum instrumental conditions for the determination of U and Th in urine by magnetic sector ICP-MS and quadrupole ICP-MS. The improved sensitivity offered by the high resolution instrument allowed quantitative determination of U and Th from a 100 μl urine sample compared with a 500 μl sample for quadrupole ICP-MS. Good correlation between the two instrumental techniques was reported (r^2 = 0.991) with a "near unity" slope and "near zero" intercept. The reported LODs for U and Th isotopes were below 3 ng l^{-1} with the magnetic sector instrument and 4 ng l^{-1} with the quadrupole instrument. The methods were used to determine levels of actinides in urine samples from firefighters exposed to smoke and particulates.

Haldimann and colleagues[189] developed a simple method for the determination of *U in urine by ICP-MS*. Quantitative determination was achieved using ID measurement with ^{233}U spiked in diluted urine samples. The authors used a new design of concentric flow nebuliser and mini-cyclonic spray chamber with a sample uptake rate of 3 ml min^{-1} to reduce matrix interferences and salt deposition at the interface. They evaluated the method by analysing NIST urine CRM 2670, which has published values for U determined by TIMS and α-spectrometry. The method was used to investigate potential exposure to U in UNHCR staff employed in Western Kosovo. Ough *et al.*[190] used both ICP-MS and INAA to determine U concentrations in urine and hair samples from Canadian forces personnel who had served in the Gulf war and Kosovo, as part of a biomonitoring programme. The total U concentrations in 24 h urine collections were determined by both techniques at independent laboratories. A mean urine U concentration of 4.5 ng l^{-1} was reported using ICP-MS compared with a mean value of 17 ng l^{-1} using INAA. The total concentrations of U in the urine samples were too low for isotope ratios to be determined. Isotope ratio measurements were performed on hair samples and the ratios determined were distributed around the natural ^{235}U:^{238}U ratio of 137.8.

Zarkadas *et al.*[61] developed a method for the separation and preconcentration of U from urine for quantitative determination by TXRF. The authors reported that the method was sufficiently sensitive to monitor U intake above normal levels. Truscott and colleagues[28] also developed a method for the separation of *actinides from environmental and biological matrices* for determination by HR-ICP-MS. In their approach, actinides were separated both from the matrix and from each other by high performance chelation ion chromatography on a polystyrene column dynamically loaded with 0.1 mM dipicolinic acid. With optimised chromatographic conditions U was separated from Pu. The authors also noted that the column exhibited selectivity for different oxidation states of Np, Pu and U. Reported LODs were 12 fg, 8 fg and 4 fg for ^{237}Np, ^{239}Pu and ^{241}Am, respectively.

1.9.25 Vanadium. Azay *et al.*[191] used ETAAS to determine V in blood in a study to examine the *oral bioavailability and pharmacokinetics of V in rats* following administration of vanadyl sulfate as an antidiabetic agent. Following either intravenous bolus injection or oral gavage, disposition of V was best described by a three-compartment model and absorption by a zero-order rate process. The calculated absolute bioavailabilities for two oral doses of 15.12 and 7.56 mg kg^{-1} body weight determined from area under the curve models were 12.5% and 16.8%, respectively, which the authors noted were higher than values generally reported in the literature.

Heinemann *et al.*[192] investigated the *binding of V^{IV} to proteins* in fresh frozen plasma (FFP) and purified solutions of human serum albumin (HSA) and transferrin (TF). Unbound V was separated from protein-bound V ions by ultrafiltration, and both 'free' and total V determined by ETAAS. The binding capacity of HSA was about 1000-fold less than that of FFP or TF. Binding of V to both FFP and TF was described by both saturable and additional non-saturable binding. The authors hypothesised that V predominantly bound to plasma TF and that, given the high binding capacity of TF compared with HSA, the amount of V delivered by administration of HSA infusion solutions is unlikely to be of toxicological importance.

Organometallic V^{IV} complexes, vanadocenes, have been identified as novel experimental contraceptives, in view of their spermicidal activity. D'Cruz *et al.*[193,194] investigated the subchronic toxicity of vanadocene dithiocarbamate and vanadocene acetlyacetonato monotriflate, in mice. Female mice were administered the compounds intravaginally at doses nearly 1200–5000 times greater than the *in vitro* spermicidal EC50 (effective concentration) value. Following treatment, blood samples were taken for measurement of haematological and clinical chemistry parameters. Microscopic examination of stained tissue samples was undertaken and tissue V concentrations were determined by ETAAS. Neither haematological and blood chemistry profiles nor histological examination revealed any treatment-related toxicity. All tissue V concentrations were less than 1 μg g^{-1}. The authors concluded that these vanadocenes may have clinical application as safe vaginal spermicidal contraceptives.

1.9.26 Zinc. *The role of Zn in prostate cancer* was investigated by Ide-Ektessabi *et al.*[40] who used XRF with a synchrotron radiation microbeam to determine both the concentration and distribution of Zn in normal and cancerous prostate tissue. Zinc levels determined in the stroma of cancerous tissue ranged from 44 to 713 ppm compared with a much narrower range of 101–180 ppm in the stroma of normal prostate tissue. Laursen *et al.*[65] also used XRF to determine Zn concentrations in autopsy liver tissue from Greenlandic Inuits and Danes. The authors observed no significant difference in liver Zn levels between the two populations. The median liver Zn concentration in the Inuit subjects was 3.809 mmol kg^{-1} dry weight compared with a median value of 3.992 mmol kg^{-1} for the Danish group. They did note a positive correlation between liver Zn and age in Danish women that was not found in either Danish men or the Inuit population. Robertson *et al.*[42] used micro-PIXE to identify significantly elevated concentrations of Zn in senile plaques of brain tissue from Alzheimer's disease patients. The authors also discussed the potential of LA-ICP-MS as a complimentary microprobe technique for distribution analysis of elements in brain tissue.

2 Analysis of foods and beverages

This report reviews *developments for the measurement of major and trace elements in foods, beverages, whole diets and related samples* such as food and herbal supplements. Table 2 provides an extensive summary of publications, including many that are not directly cited here in the text.

Reviews of methods suitable for the characterisation of foods and to detect adulteration include the 2002 Atomic Spectrometry Update,[1] which is restricted to atomic spectrometry, while other techniques are mentioned in more general presentations.[195,196] One refers to methods applied to the analysis of wines[197] while another reviews methods to determine Al in tea.[198]

Our last Update[1] drew attention to studies involving *organically produced foods* and one further publication[199] has since appeared. Tissues were taken from cattle maintained under conventional conditions in which mineral fertilisers were used and matched animals reared under 'organic' conditions. Lower Cd concentrations were measured in the liver, kidney and mammary tissue of the 'organic' cows, but Cd in muscle was not different. Zinc concentrations were lower in kidney and higher in muscle of the 'organic' cattle.

Genetic influences on the accumulation of metals were also reported. Strains of durum wheat that were identical except for the ability to accumulate Cd were grown in an experimental situation. Yield was identical in the high- and low-Cd strains, and while there were differences in the concentrations of other elements these were not associated with the Cd content, and it was concluded that the low-Cd allele is specific for Cd.[200] Genetic modification was investigated in the Se-accumulator Indian mustard. A variety with over-expression of the enzyme responsible for the incorporation of organoselenium compounds into protein did not accumulate more Se than did the wild-type but was able to convert the inorganic Se into methylselenocysteine with much greater effectiveness.[201]

2.1 Sampling and sample preconcentration

Food samples with *high proportions of fat or fibre are difficult to homogenise.* It was shown that slurries formed after cryogenic grinding gave reproducible data. Samples were simply cut into small pieces and ground in liquid N_2 for 2 min and analysed by ETAAS for Cd and Pb.[202] The same workers also used cryogenic grinding to homogenise breakfast cereals.[203] Another simple procedure for preparing samples involves forming an emulsion with a suitable medium. Benzo *et al.*[204] successfully used an emulsion (35%) of margarine with Tween 80. Concentrations of Fe and Ni determined by ICP-AES were similar to those obtained after a lengthy digestion method. Four surfactants were investigated in another study in which 'microemulsions' were prepared for measuring Mn in different foods.[205]

2.1.1 Extraction. A number of interesting studies were reported in which *simple rapid extraction procedures* were exploited and/or compared. Proteolytic enzymes enhanced the extraction of Se from various food types prior to speciation and measurement.[206–208] A combination of protease VIII and lipase VII was particularly effective. Ultrasonic energy to increase extraction speed and efficiency is regularly reported,[209,210] but in a novel application Cu was extracted from solid mussel samples using an ultrasound-assisted on-line flow injection manifold connected to an FAA spectrometer.[211] Alternatively, microwave energy may be used to promote extraction. Several experiments, with up to 15 different extraction methods compared, have been reported and the use of microwaves generally provided the most favourable results.[112,212–214] The detailed work of Brisbin and Caruso[112] included investigating the influence of the solvent used on the extraction of different inorganic and organic species for a range of different elements.

2.1.2 Digestion. Sample preparation by digestion of organic material with concentrated acid remains hugely popular. Methods are straightforward and there are very few new

developments but it is worth noting the use of *ashing aids to deal with difficult sample types*. To measure Cd and Pb in sunflower oil Cruz *et al.*[215] included V_2O_5, while complete conversion of AB and AC in fish tissue to As^{III} was accomplished with the use of $K_2S_2O_8$.[216] In a comparative study of acid extraction, acid digestion and dry ashing of total diets, the extraction procedure was recommended as it was fast, simple and gave accurate results for the measurement of Ca, Cu and Fe.[212]

2.1.3 Preconcentration. *Novel approaches to preconcentration* are always of interest and several have been reported. Cryogenic trapping and GC separation of Hg species was accomplished in the same capillary column by Dietz *et al.*[155] Dimethylmercury, methylmercury and Hg^{II} were measured in fish with LODs of 6.0, 0.95 and 1.25 ng l^{-1}, respectively. Gold wire has long been used to trap and concentrate Hg vapour but it has been shown that the species SeH_2 decomposes to Se^0 and may be collected on gold wire heated to 200 °C. With subsequent heating to 600 °C, the Se was released into a stream of H_2 and the hydride then formed was measured by AFS or AAS. The LOD, with a 5 min collection time, was 5 pg ml^{-1} and Se was determined in mineral water samples.[217] In two papers by He *et al.*[218,219] concentrations of Cr and Pb in drinking water were enhanced by the use of an electrostacking technique, as part of what was described as an electrokinetic flow analysis system. Optimum parameters were derived for sample tube cross-section and stacking time, and with ETAAS for measurement LODs were in the low ng l^{-1} range. Procedures involving extraction of analyte into micelles of non-ionic surfactant (cloud point extraction) were exploited for the preconcentration of Hg in water[220] and speciation of Fe (see 2.4 below).

Methods involving *analyte trapping onto resins or functionalised support materials* within FI systems are now so regularly reported that they may be regarded as routine. Among the many reports in this vein one included a comparison of four sorbents used to retain Pb from tap water. Sorption capacity, loading half times and tolerance to major ions were investigated and the LODs were given as 2.44–7.87 ng ml^{-1}.[221] Li *et al.*[222] reported a multiplex system where repeated short samplings were loaded onto an APDC trap. This permitted much greater retention efficiency than with a single loading over a prolonged time, and an extended linear range. With samples of water, herbal medicines and tea, the enhancement factor for Pb was 57 and the LOD was 8 μg l^{-1}. In two related papers Cd and Pb in wine were measured by ICP-AES. The respective enhancement factors and LODs were very impressive at 216 and 5 ng l^{-1} for Cd, and 225 and 0.15 μg l^{-1} for Pb.[223,224] In a rather more unconventional analysis, Cu, Fe and Zn were measured in rum by EDXRF with ng ml^{-1} LODs after APDC preconcentration.[225]

It is not usual to have to determine *Tl in foods and beverages* but a method for measurement in wine was reported.[226] Samples were digested with HNO_3 and H_2O_2 and the Tl extracted in IBMK for ETAAS. With a 50-fold preconcentration, the LOD was 0.05 μg l^{-1}.

2.2 Speciation

Methods for the chromatographic separation of the As and Se species found in biological specimens have reached a sufficient stage of maturity that minimal details are now included in many publications. One example of this trend is *a commercially available "Speciation Kit"* available for the separation of As^{III}, As^{V}, MMA and DMA in drinking water.[227] Notwithstanding these achievements, some workers continue to re-evaluate the basic chromatography, *e.g.*, to measure As in apple extracts.[210] However, a large proportion of the work involving LC seen in the last year focuses on either an innovation in the sample preparation or on the detail and significance of the analytical results. Of five methods compared for extracting Se species from mushrooms, a procedure involving extraction with H_2O and digestion with pepsin and trypsin was most effective.[207] Haem and non-haem-Fe in cooked or uncooked meat, separated by HPLC-ICP-MS, indicated that much of the haem-Fe was lost on heating. However, a spectrophotometric procedure showed no such loss and it was inferred that the extraction method for HPLC was inappropriate.[228] Thirty selenocompounds from yeast extracts were separated, although not all were identified, using sequential SEC, anion-exchange and cation-exchange reactions. This so-called 'three-dimensional LC' was linked to an ES-MS for detection.[229] Moving away from LC, Hg in fish was speciated by GC in which the capillary column was employed for the derivatisation, cryogenic trapping (see 2.1.3, above) and the separation prior to detection by MIP-AES.[155] Separate measurement of Cr^{III} and Cr^{VI} is important because of the carcinogenicity of Cr^{VI}. This objective was realised in water samples by adsorption onto neutral alumina followed by elution of Cr^{III} with 4 M HNO_3 and Cr^{VI} with 1 M NH_4OH. The Cr was measured by ETAAS with an LOD of 0.01 μg l^{-1}.[230]

2.3 Applications using hydride generation

While HG continues to be popular most of the interesting aspects concern the steps involved in sample pretreatment and speciation. However, attention is drawn to two studies. The first involved measurement of arsenosugars in aqueous extracts of oysters.[231] The authors found that results given by LC-ES-MS were about half those obtained when LC-HG-AFS was used. The discrepancy was attributed to a severe matrix effect and was abolished by using standard additions calibration, or by employing an extensive clean up with anion-exchange and SEC, for LC-ES-MS. In a particularly unusual application, *Zn was measured in foods as the hydride derivative by AFS.*[232] Samples were taken into cetyltrimethylammonium bromide micelles and these organised media led to improved hydride generation compared with an aqueous medium. Satisfactory results were reported for CRMs.

2.4 Applications using flame atomic absorption spectrometry

In recent years developments involving FAAS have mainly been consequent upon *on-line FI systems* for sample preconcentration. Examples of this work have been seen again during the last year, including one where Ni was determined in food samples after enrichment using an Amberlite XAD-2 column loaded with 2-(2-benzothiazoylazo)-2-*p*-cresol. The LOD was 1.1 μg l^{-1}.[233]

However, there are a number of other interesting developments for flame analysis reported in the last year. Barium in mineral water was measured with an LOD of 0.034 mg l^{-1} by using an O_2-enriched air–C_2H_2 flame.[234] Maximum sensitivity was achieved with O_2 at 52% in the mixed gas and the O_2 : C_2H_2 ratio at 0.72. A water-cooled quartz atom-trap was successfully employed to measure Pb in Chinese herbs; conditions such as trap position, flame composition and sampling time were optimised.[235] Flores *et al.* have developed a *most original accessory* in which 0.05–0.5 mg of dried powdered sample (<80 μm particle size) was placed in a polyethylene vial connected to a glass chamber. Air flowing through this device produced a dry aerosol, which was conducted to T-shaped quartz tube mounted on the burner. A transient atomic vapour was produced and the non-atomic absorption was very low with a characteristic mass for Cu of 1.5 ng.[85] Finally, properties associated with structured sample solutions, which were aspirated into conventional burner–flame systems, were exploited by two groups of workers. With a microemulsion, Mn absorption increased by 58%,[205] while micelles of a mixture

of non-ionic surfactants were used to extract tannins and other phenolic fractions from wine to permit separate measurement of the free and tannin-bound Fe.[236]

2.5 Applications using electrothermal atomic absorption spectrometry

Measuring *mercury by ETAAS* is still an analytical challenge so that any report is worth mention. A modifier of Pd–Zr coating the furnace allowed the measurement of Hg in biological tissues, including foods. The LOD was 3 pg and analysis of CRMs gave consistent results.[237] Food colouring agents were suspended in 0.1% Triton X-100–1% HNO_3–2% $KMnO_4$–3% $Ag(NO_3)_2$ and added to the furnace. A fast heating programme was used to avoid losses by volatilisation and the Hg LOD was 59 pg. Results compared well with those obtained by other methods and with a CRM.[238] A fast heating programme was also employed as part of a rapid procedure to determine Se in seafoods.[209] Speed was attained by ultrasonic-acceleration of extraction, aqueous standards for calibration and omission of the pyrolysis step from the measurement. With a Pd modifier valid results were obtained for two CRMs.

Attempts to find *ideal chemical modifiers* represent a constant source of investigation. In a systematic study of the difficult task of measuring As in sugar, pyrolysis/atomisation curves were prepared with additions of $Pd(NO_3)_2$, $Pd(NO_3)_2$–$Mg(NO_3)_2$ and $Ni(NO_3)_2$. Different optimum conditions were obtained when either sugar slurries (an unusual sample type as sugar is normally very soluble) or digests were analysed but the authors concluded that Pd provided the best modifier for this application.[239] A novel modifier with $Ni(NO_3)_2$ and $Sr(NO_3)_2$ mixed together was recommended when Se was measured in wine.[240] The authors suggested that the mass required was less than with other published modifier solutions and was equally as effective. It was also recommended that, for complete elimination of interferences from SO_4^{2-} and PO_4^{3-}, the samples should be digested and the Se extracted into IBMK as the APDC complex. Modifiers involving Ir have been proposed recently as this can be applied to give a more or less permanent coating. Grinberg *et al.* employed Ir in a FAPES procedure to determine Cd and Pb in various sample types. The authors optimised the coating procedure, atomisation and FAPES parameters. LODs were between 2 and 4 ng g^{-1}.[88]

Features of *non-graphite furnaces* are occasionally presented and, with a molybdenum atomiser used to determine Mn in herbal medicines, an LOD of 69 fg was obtained. Samples were prepared as slurries in 10% glycerol, which also abolished matrix interferences.[107] Conditions for the simultaneous measurement of Cd and Pb in wine were established using various modifiers of which 5 μg Pd + 3 μg Mg was found to be best without the accumulation of carbonaceous residues. Wines were analysed without any pretreatment.[241] In a more ambitious procedure the same authors determined As, Cu, Mn, Sb and Se simultaneously in mineral water.[242] They again investigated different modifiers, reaching the same conclusion. The compromise ash and atomise temperatures were 1400 and 2100 °C, and results of the analysis of an SRM were in agreement with certified values.

2.6 Applications using inductively coupled plasma mass spectrometry

Relatively little new work is reported this year and, as in the last Update,[1] it is noted that *multi-element analysis appears to represent a minor interest*. However, in one extensive, systematic project the measurement of 15 elements in cereals, seafoods and meat was investigated. Matrix interferences were determined and spectral interferences due to C, Ca and Cl were studied. Techniques to overcome these interferences were applied and a standard protocol to ensure accurate results was written.[243] A method that has 'something for everyone' might be one way to describe the procedure of Ho and Jiang to measure Cd, Cr, Pb and Zn in milk powder.[244] Samples were prepared as slurries with ultrasonic mixing and introduced into the plasma by ETV with ascorbic acid used as a modifier. Within the dynamic reaction cell, interferences on Cr and Zn were reduced by including NH_3 as the cell gas. Finally, ID was used to accommodate matrix effects—although it was also stated that standard additions were used. The authors report that results for CRMs agreed with the certified values. A method with no sample preparation was reported for measuring methylmercury and Hg^{II} in biological materials.[150] ETV of powdered CRMs weighed into a graphite furnace 'boat' was used for sample introduction. Different temperatures provided separate vaporisation of the Hg species. Calibration by ID involved the preparation of a permeation tube loaded with ^{200}Hg. Emission of the isotope was previously determined by CV-AAS and CV-AFS.

Isotopic analysis to aid the characterisation of wine is no longer novel but the approach depends on reliable precision. ^{87}Sr and ^{86}Sr were measured with precision values of 0.002–0.003% using an SF-mass analyser. It was necessary to remove Rb by cation-exchange chromatography to avoid the ^{87}Rb interference.[245] Iodine as iodide is unstable in HNO_3 so that inaccurate results may be obtained when samples are prepared by acid digestion. This problem was overcome by addition of 3% NH_4OH to digests of fish from the Barents, Norwegian and North Seas.[246] Mass cut-off filters in the HPLC-ICP-MS were used to investigate how much of the Se extracted from oyster samples remained bound to protein after enzymatic hydrolysis. By separating the forms with M_r greater than 10 kDa it was shown that destruction of protein was more effective in the soluble extract compared with the insoluble residue.[206]

2.7 Applications using other analytical techniques

In a most unusual piece of work the *measurement of iron and manganese by a cold vapour technique is reported* (the complete details were not available for review).[247] The authors analysed a number of biscuits, including some that were enriched with whole grain flour or other additions. The more orthodox use of the CV technique involves measuring Hg and interesting developments feature FI systems for preconcentration. Martinez and colleagues used 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (PADAP) in a knotted reactor with CVAAS. A 25-fold increase in concentration was achieved, and Hg in water was measured with an LOD of 5 ng l^{-1} from a 25 ml sample.[248] With ICP-AES detection, and with the sample incorporated into micelles of polyethyleneglycol mono-*p*-nonylphenyl ether, the same FI-knotted reactor CV system yielded an LOD of 4 ng l^{-1} with 50 ml of sample.[220] As described above (2.1.3 and 2.2), an MIP-AES detector was used to measure fish Hg species preconcentrated and separated by capillary GC.[155] Although ICP-AES is a multi-element technique, just as for ICP-MS, few publications were seen that exploit this feature. With their same PADAP knotted reactor Martinez *et al.* reported a total enrichment of 216-fold when measuring Cd in wine.[223] A novel piece of work involved generation of volatile bromides with Se^{IV} and Se^{VI}, which were separately measured by ICP-AES.[249]

Several applications involving either *XRF or PIXE for the analysis of foods* and beverages were published in the last year. An unlikely method that determined Se in onions and potatoes used acid digestion, co-precipitation with Te and ^{75}Se, dissolution and deposition onto polycarbonate for PIXE analysis.[250] The method appears far too impractical for real use. PIXE was also investigated for the fast determination of Pb in wine. As the technique does not have the required inherent sensitivity, 5 ml samples were evaporated beneath an IR lamp until an LOD of 50 ppb was met.[251] Measurement of

Cr in medicinal herbs[252] and Cu, Fe and Zn in rum[225] by XRF was reported. Preconcentration steps were necessary to obtain any results. In one truly multi-element application, 22 elements were determined in conventional and herbal teas by EDXRF.[253]

2.8 Progress for individual elements

2.8.1 Arsenic. Total As concentrations in muscle, liver, kidney and lung from sperm whale were from 0.3 to 3.0 μg g^{-1} (dry weight) and when the species were separated most of the As was present as AB. Small amounts of DMA and AC were also detected, together with trimethylarsoniopropionate, which has previously been detected on only one other occasion.[114] In an investigation of the possible impact of *contaminated soil and ground water* on As in human milk, samples were collected from women living in three areas of Germany. Specimens were collected before and after nursing for up to 90 days *post partum*. A total of 187 samples were analysed and the As was <0.3 μg l^{-1} in 154. Results from the three regions (contaminated, rural and city) were not different and it was calculated that the total daily intake is 0.02–0.06 μg kg^{-1} body weight.[126] Contamination of drinking water in West Bengal attracts considerable research interest from all around the world. A combined Japanese–German study employed a rapid HPLC-ICP-MS procedure to identify the As species in samples from one district. In addition to As^{III} and As^{V}, DMA and MMA were detected at low concentrations (<2.1 ppb) in most samples.[254] The methylated species were said to have previously been undetected in drinking water but in previous Updates we have referred to reports where these species were identified.

2.8.2 Cadmium. The impressive sensitivity associated with ETAAS for Cd ensures that the technique continues to be widely used for this determination.[255,256] For the apparently simple *analysis of wine* diluted 1 + 1 with 0.056 mol l^{-1} HNO_3, a mixed chemical modifier with Mg and Pd was used together with a two step pyrolysis programme.[241] The reported LOD of 0.03 μg l^{-1} was surpassed, however, by a procedure involving ICP-AES with preconcentration in a knotted reactor containing PADAP (see 2.7, above). The Cd in wine was measured with an LOD of 5 ng l^{-1}.[223]

2.8.3 Lead. Measurement of Pb in wine featured in a project from the Institute of Reference Materials and Measurements. Samples were analysed by ID-ICP-MS and the report of the data included assessment of the factors contributing to the measurement uncertainty with the major contribution attributed to the measured sample homogeneity correction factor.[257] Like Cd, *ETAAS continues to be the technique employed in most of the studies* seen this year. However, a collection of Chinese herbs were analysed using FAAS with a water-cooled quartz atom trap.[235] The LOD was superior to that of conventional FAAS by more than 10 fold.

2.8.4 Mercury. Improvements to the classical vapour generation procedures were reported by one group who applied on-line preconcentration for measuring Hg in water by both AAS and MIP-AES. A detection limit as low as 4 ng l^{-1} was achieved.[220,248] Good results are now obtained using ETAAS, due to the development of suitable modifiers such as $KMnO_4$. A range of different foods were analysed and according to the procedures used the absolute LODs were from 33 to 53 pg.[237,238] Perhaps *the most innovative work* was that of Dietz *et al.*[155] in which capillary GC, with detection by MIP-AES, provided for preconcentration, separation of dimethylmercury, methylmercury and Hg^{II}, and ng l^{-1} detection limits in oyster and tuna fish.

2.8.5 Selenium. While most attention was focussed on speciation, some developments in the measurement of total Se were introduced. The philosophy of *very short heating programmes for ETAAS* was shown to be applicable for the analysis of seafoods. The pyrolysis step was omitted and aqueous standards were used for calibration. With a Pd modifier the LOD was 0.16 μg g^{-1} and precision was 3–12% (RSD).[209] Separation of Se species by HPLC continues to be described[206,207] and organoselenium compounds in Indian mustard were identified by reverse phase HPLC-ICP-MS but then measured using ES-quadrupole time-of-flight MS. Increased amounts of methylselenocysteine were found in genetically modified plants where there was overexpression of the enzyme So-cysteine methyltransferase.[201]

The advantages of *gaseous sample introduction* in atomic spectrometry were very nicely reviewed in the introduction to a paper by Lopez-Molinero *et al.*[249] Alternatives to hydride generation and cold vapour generation were mentioned and then these workers described a procedure that involved measurement of Se^{IV} and Se^{VI} in mineral supplements as their volatile Br compounds, with subsequent measurement by ICP-AES.

2.9 Single and multi-element analysis of foods and beverages

In previous Updates we have noted that measuring minerals and trace elements may be useful to help identify the location in which wine was produced. This principle has since been extended to other food types. Four varieties of avocado from different parts of the Canary Islands were analysed for B, Ca, Cu, Fe, K, Mg, Mn, Na, P and Zn. The *area of origin was reflected in different element concentrations within the same variety* but there were also differences between the four varieties, indicating that careful interpretation of data is important.[258] Raisins imported into Canada from Australia, Chile, Iran, Mexico, South Africa and Turkey were investigated to determine their contribution to the intake of Pb.[259] Most contained low concentrations, 0.005 to 0.010 mg kg^{-1}, but Turkish raisins had Pb at 0.056 to 3.1 mg kg^{-1}. This Pb was traced to the use of a contaminated fungicide. Samples of liver and kidney from Icelandic lamb were analysed for six elements. Concentrations of Cd, Cu, Fe and Hg differed among different areas of the island but none was high except for Fe, which showed a pattern of distribution that resembled that of moss—an indicator of airborne deposition. It was also noted that recent volcanic activity had not influenced concentrations of Cd and Hg.[260]

Herbs and medicines from China appear to be generating much interest and the number of reports of where these and similar specimens have been analysed is increasing rapidly. This review does not include a systematic discussion of the recent publications but simply draws attention to the trend. Work includes assessment of potential toxicity due to the natural content or contamination of elements such as Pb,[235] and the possible therapeutic properties associated with, *e.g.*, Ca, Cu, Fe, Mg and Zn.[108]

2.9.1 Dietary intake studies. Several *duplicate diet studies* were published in this review period. A German group reported the Cd intakes of children and adults living in an industrial area and on an island in the North Sea.[261] They concluded that dietary levels were higher in the industrial city and should be reduced. In a follow up to work with Cd, which was mentioned in our last Update,[1] the intakes of As in Belgium were reported.[262] The highest concentrations in individual foods were in fish and rice but the mean intake was below 30 μg d^{-1}. In a very specific study, 11 elements were determined in diets from pregnant and non-pregnant women (migrants into Australia), human milk and formulas. Data were compared with the results from a similar study in the USA. Amounts were

generally lower than in the USA and there was some concern that intakes of Ca, Fe and Zn were inadequate.[263] In two separate publications the daily dietary intake of Cr and the Cr concentration in typical Spanish feeds were reported.[264,265] From the duplicate diet data, intakes ranged from 9.39 to 205.16 μg d^{-1} (mean = 100). Highest concentrations were in seafoods, vegetables and cereals, dairy products and olive oils. Cr concentrations in Mexican foods were similar to those seen in Spain, although the mean daily intake was lower at 30.43 μg d^{-1}.[266] An analysis of West African foods revealed a huge range of Ca concentrations, 3–3630 mg per 100 g dry weight, with highest amounts in vegetable leaves.[267] Yet another enormous study of Cd in Japanese foods was presented and showed that major contributions (up to 0.38 μg g^{-1}) come from cereals, shellfish and pulses.[256] Analysis of burgers, pizza and French fries indicated that these fast food products offer useful contributions to daily dietary Ca, Fe and Mg.[268]

2.9.2 Human milk and infant formulae. Since 1984, Se has been added to fertilisers used in Finland to increase the concentrations in foods grown in naturally Se-poor soils. The impact of this intervention on concentrations of Cd, Cu, Se and Zn in *human milk* was investigated between 1987 and 1995 and has now been published.[269] The study also included the location, smoking habits, fish eating and age and parity of the mothers. The interactions were complex and included an effect of the high natural Cu content of soils in one area. However, Se concentrations of human milk increased (16.4–18.9 μg l^{-1}) as a consequence of the supplementation while Cd, Cu and Zn were reduced. Studies to examine As in human milk and the concentrations of 11 other elements in samples from Australian immigrants were discussed in sections 2.8.1 and 2.9.1, above.

Measurements of Cd and Pb in infant formulae showed differences related to the types of product: beginner, continuation, special infant-hypoallergenic, special infant-lactose-free, special infant-vegetable base, special infant-others. None of the formulae made an appreciable contribution towards the provisional tolerable weekly intake.[255,270] Fortified breast milk provided to extremely low birth weight infants, and widely used throughout Europe, failed to provide the requirements for Ca, Mg and P.[12] In *a comparative study of infant formulae* purchased in Nigeria, the United Kingdom and the United States of America, 26 elements were measured. The drinking water limit values for Al, Ba and Tl were exceeded in some brands while the supply of essential elements were inadequate in many examples.[271]

2.9.3 Milk and dairy products. *Camel milk* has been compared with human and cow's milk and was found to be an acceptable source of trace elements. Concentrations of Fe and Mn were especially high while the amounts of Cu, Se and Zn were at least as good as in other milk types.[272] Using techniques such as selective protein precipitation and enzymatic hydrolysis the binding of Ca, Fe, Mg and Zn to bovine milk proteins was investigated.[273] It appeared that Ca, Mg and Zn were associated with colloidal calcium phosphate while Fe was attached to a casein polypeptide chain.

2.9.4 Wheat, flour and rice. In a very prolonged investigation, Cd and eight other elements were measured in wheat and rye flours and in wheat bran for 15 years.[274] *Temporal changes were reported* involving all sample types with concentrations of some elements gradually increasing, some decreasing while Cd in flours increased and then fell again. No explanation for these trends was proposed. The concentrations of Cr and Ni were shown to be associated with the amount of bran, and hence the origin of the wheat flour. Texture, however, a feature of the milling process, did not correlate with these elements.[275] The genetic component to accumulation of Cd in durum wheat[200] was discussed above, in the introduction to the section on foods and beverages in this review.

2.9.5 Fish and seafood. With the ready availability of CRMs derived from fish and seafood, new analytical developments are often validated by analysis of such samples. Such work, using lyophilised and finely powdered materials, however, is not especially relevant to a discussion of *real samples*. Fish species caught in the Barents, Norwegian and North Seas were taken for measurement of I by ICP-MS. Concentrations ranged from (mean) 0.07 mg kg^{-1} wet weight in ling to 2.5 mg kg^{-1} wet weight in cod. Intra-species variation was also quite high.[246] An analysis of sardines canned in either tomato sauce or soyabean oil was reported from Brazil.[276] Eight elements (Cd, Cr, Cu, Fe, Mn, Pb, Sn and Zn) were measured and those at the highest concentrations were Fe and Zn. Generally the highest con- centrations were in fish canned in tomato sauce. However, only Cr was consistently above the limit value although the Pb in one brand also exceeded the permissible concentration. Differences were attributed to the canning process and the quality of the sardines.

The importance of fish as a dietary source of Hg, and the potentially harmful effects during pregnancy and childhood, has been much stated in recent years. *Swordfish is known to be an accumulator of mercury* and various authorities have produced recommendations as to how much may safely be consumed. Mendez *et al.*,[277] from Uruguay, offer data to suggest that the situation may not be as straightforward as is sometimes presented. They found that Hg in the edible part of swordfish was from 0.04 to 2.21 mg kg^{-1} but that there were really two subsets of data dependent on the size of the fish. Specimens less than 100 kg had low concentrations of Hg and could be considered safe for eating but that larger fish, where bioaccumulation was greater, should be avoided. Work from an Italian laboratory appears to be less worrying. In different fish types the Hg concentrations were from 0.057 (sole) to 0.579 (swordfish) mg kg^{-1}.[278] However, the size of the fish and where they were caught are not known. Shellfish had much lower concentrations of Hg. The same samples were also analysed for Se and concentrations were much higher than for Hg and were similar in fish and shellfish.

2.9.6 Water. Analysis of *bottled mineral waters* often demonstrate that these beverages fail to meet the standards applied to drinking water. Forte *et al.* opted to determine U in samples obtained in northern Italy[279] while Cr was measured in a Spanish investigation[219] and As, Cu, Mn, Sb and Se were determined in samples from Brazil.[242] A sensitive procedure involving an FI system for preconcentration was employed to measure Hg in tap water in Argentina,[220] but the most detailed investigation was that in which As species were determined in drinking water in West Bengal, India.[254]

2.9.7 Wine and beer. *Most of the work involving these samples was directed to the analysis of wines* but in one study ten brands of rum were taken for measurement of Cu, Fe and Zn. In two of the rums, the Cu concentrations exceeded the limit permitted in Brazil.[225] Elaborate procedures were developed for separation and measurement of total, free- and the tannin-bound Fe in wines.[256] The ^{87}Sr: ^{86}Sr ratios in wine of different origins were quite different dependent on whether they were derived from basaltic, mixed or granitic soils.[245]

2.9.8 Reference materials and collaborative trials. There is little to review relating to these topics. The report of *the 16th International Measurement Evaluation Programme (IMEP), involving the determination of lead in wine, was published.*[257] Concentrations of Pb and the measurement uncertainties were reported by the 129 participants, and results were from <1 to

Table 2 Analysis of foods and beverages

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Al	Fruit juice, soft drinks, water	AA;ETA;L	Samples were digested with HNO_3 V_2O_5 prior to measurement	328
Al	Beer, beer ingredients	AA;ETA;L, Sl	Solid samples were introduced as suspensions following treatment with a solution containing H_2O_2 HNO_3 $NH_4H_2PO_4$. Liquid samples were pipetted directly	329
As	Well water	MS;ICP;FI	As^{III}, As^{V}, DMA and MMA were determined in samples from West Bengal	254
As	Water	MS;ICP;HPLC	Analytical performance characteristics were calculated for the determination of As^{III}, As^{V}, MMA and DMA	227
As	Human milk	AA;Hy;L	The milk from 32 mothers was analysed in Germany as part of a study of possible contamination arising from WW II chemical weapons. Happily, no elevated levels were found	126
As	Vegetables	-;-;-	The As uptake by vegetables in an area of Chile with high soil concentrations was found to pose no health risk	330
As	Foods	AA;Hy;L	Samples were digested using HNO_3 H_2O_2, excess oxidant removed by addition of HCl and urea and KI used to reduce As^{V} to As^{III}. The LOD was 0.6 μg l^{-1}	331
As	Seafood	AA;Hy;HPLC	A coupled HPLC microwave oven HGAAS method for speciating As^{III}, As^{V}, MMA, DMA, AB and AC was described. During the microwave step $K_2S_2O_8$ as oxidising agent was used to enhance the efficiency of conversion of AB and AC into As^{V}	216
As	Sugar	AA;ETA;L	Optimum conditions for a number of chemical modifiers were identified (in Portuguese)	239
As	Food colours	AA;ETA;Sl	0.025 0.15 g of colorant was weighed, and 10 ml of 0.1% m/v Triton X-100 50% v/v H_2O_2 1% v/v HNO_3, 1 drop of silicon antifoam and the corresponding matrix modifier (0.3% m/v Ni for As and 1% m/v $NH_4H_2PO_4$ for Cd and Pb) added. The LODs were 33, 0.8 and 11 pg for As, Cd and Pb	332
As	Apple	MS;ICP;L	Extraction procedures and HPLC separations were evaluated for As speciation	210
As	Coffee	AE;ICP;HG	Samples were digested using HNO_3 H_2O_2 in a microwave oven and As and Se determined	333
As	Oyster	MS;ES;HPLC AF;Hy;L	2 techniques were used to quantify an arsenosugar and analytical limitations discussed	231
As	Seafood	MS;ICP;HPLC MS;ES;HPLC	The chemical stability of 4 arsenosugars in simulated gastric juice and acidic extraction regimes was investigated	334
As	Marine tissues	MS;ICP;HPLC	As species were extracted from freeze-dried tissues using 50% (v/v) CH_3OH H_2O in a microwave oven heated to 70 75 °C	113
Ba	Mineral water	AA;F, O_2 enriched air C_2H_2;L	An O_2:C_2H_2 ratio of 0.72 gave increased sensitivity and yielded an LOD of 0.034 mg l^{-1}	234
Ca	Grape juice, wine	AA;F;L	Methods evaluated included dealcoholisation, dry mineralisation, and wet mineralisation with heating by using different acids and/or mixtures of acids. The analytical performance of the methods were established	335
Ca	Human milk, blood, urine, faeces	AE;ICP;L	The results showed that the needs of low birth weight infants for Ca, Mg and P were not met by a human milk fortifier widely used in Europe	12
Ca	Milk products, smoked fish	AA;F, air C_2H_2;L AA;F, N_2O C_2H_2;L	Ca, Li and Sr were determined by dry ashing in a quartz crucible, followed by treatment with HCl and HNO_3	336
Ca	Weaning foods	AA;F;L	The bioavailability of Ca, Fe and Zn was calculated	337
Ca	Foods	AE;ICP;L	Results of a study to estimate Ca content of 28 West African foods were reported	267
Ca	Foods, urine	MS;ICP;L	A new method for Ca isotope ratios, using SF-ICP-MS with a shielded torch, was described. Calculation of uncertainty allowed critical parameters in the experiment to be identified	31
Cd	Beer, beer ingredients	AA;ETA;L, Sl	See Al, ref. 329	329
Cd	Wine	AA;ETA;L	A simultaneous method for Cd and Pb, based on transverse heating and Zeeman-effect ETAAS was described in detail	241
Cd	Wine	AE;ICP;FI	Cd was retained in a knotted reactor as Cd 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol, then eluted using 3 M HNO_3. Using an USN and 60 s preconcentration the LOD was 5 ng l^{-1}	223
Cd	Foods	AA;-;-	A study of adults and children in Germany showed, from a duplicate diet study, that the provisional tolerable weekly intake was being exceeded in an number of cases	261
Cd	Mussels, milk powder	AA;F;FI	Prior to column preconcentration the pH of acid digests was raised off-line to 3 5 using NH_3, then adjusted to 8 on-line using ammonium acetate buffer	338
Cd	Rice	AA;-;L	Maximum Cd, Hg and Pb levels of 178, 43.6 and 1529 μg kg^{-1}, respectively, were found in rice imported into Saudi Arabia	363
Cd	Bovine offal, muscle	AA;ETA;L	Tissues were collected from 67 animals at slaughter, the animals having been raised organically or conventionally. Significantly lower levels of Cd and Zn were found in liver and kidney samples from the organically reared cattle	199

Table 2 Analysis of foods and beverages (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Cd	Japanese foods	AA;ETA;L AA;F;L	Cd was determined in 519 foods and beverages	339
Cd	Oyster	-;-;-	The bioaccumulation of Cd, Se, and Zn in tissue of an estuarine oyster (*Crassostrea rivularis*) and a coastal oyster (*Saccostrea glomerata*) from both the dissolved and particulate phases was investigated. The study demonstrated differences in the accumulation of metals	340
Cd	Foods	AA;ETA;Sl	Samples were homogenised by cryogenic grinding, the resulting powder, 5 20 mg, transferred to the autosampler cup with 0.2% HNO_3 0.04% Triton X-100 and sonicated. An aliquot was transferred to a Rh W coated tube containing an integrated platform with a permanent tungsten carbide rhodium modifier	202
Cd	Food colours	AA;ETA;Sl	See As, ref. 332	332
Cd	Sunflower oil	AA;ETA;L	Samples were digested using HNO_3, with V_2O_5 as catalyst and Cd and Pb determined in 21 samples. Of these only one exceeded proposed EU limits	215
Cd	Durum wheat	AE;ICP;L	Durum wheat shows genetic variation for Cd concentration. A study of 5 pairs of near isogenic lines found the low Cd allele lowered Cd without altering concentrations of other elements or affecting economic traits	200
Cd	Cereals	MS;ICP;L	Japanese Cd and Pb intake from bread, noodles, rice and wheat flour was estimated	341
Cd	Cocoa	MS;ICP;SEC	15 extraction methods were investigated for the recovery of different classes of Cd and Pb species in 8 different cocoa powder samples. Cd and Pb were very firmly bound to the insoluble matrix components, yielding recoveries <20%	214
Cr	Drinking water	AA;ETA;L	A feasibility investigation was carried out on the use of bidirectional electrostacking for simultaneous separation and pre-concentration of Cr^{III} and Cr^{VI}; the LODs were 6 and 5 ng l^{-1}, respectively	219
Cr	Drinking water	AA;ETA;L	Cr^{VI} and Pb^{II} were preconcentrated for 10 min using an electrokinetic flow analysis system and a bi-directional electrostacking unit, yielding ETAAS LODs of 10 and 13 ng l^{-1}, respectively	224
Cr	Water	AA;ETA;L	Following column preconcentration, adsorbed Cr^{III} was eluted with 4 M HNO_3 and Cr^{VI} with 1.0 M NH_3 solution	230
Cr	Gastrointestinal perfusates, serum, water	AF;ETA;laser	Atomisation was performed in a commercial electrothermal atomiser, with pyrolytically coated tubes, but without platforms. Optimum ashing and atomisation temperatures were 1300 and 2500 °C, respectively. An LOD of 4 pg ml^{-1} in 20 µl of water was achieved	89
Cr	Urine, water	MS;ICP;L	The use of a dynamic reaction cell reduced isobaric interferences	32
Cr	Wheat flour	AA;ETA;Sl	Cr and Ni were determined by slurry atomisation (3% w/v in 15% HNO_3 10% H_2O_2). Differences between sample arose from geographical origin, rather than being a function of the milling process	275
Cr	Foods	AA;ETA;L	Cr was determined in 20 food types from Northern Mexico. The highest levels were recorded in cheese (in Spanish)	266
Cr	Foods	AA;ETA;L	A survey of food from Greece showed meat, fish, cereals and pulses to be good sources of Cr	342
Cu	Human milk, cow's milk infant formula	AA;-;-	Differences in Cu and Zn levels due to home preparation were investigated	343
Cu	Beer, beer ingredients	AA;ETA;L,Sl	See Al, ref. 329	329
Cu	Rum	EDXRF;-;L	Following preconcentration using APDC, Cu, Fe and Zn were determined in Brazilian rum. LODs were in the ng ml^{-1} range	225
Cu	Bovine liver	AA;F, air C_2H_2;S	Sample, 0.05 0.50 mg, was weighed directly into a small polyethylene vial connected to a glass chamber. Air carried the sample as a dry aerosol to a T-shaped quartz cell positioned above the burner in the optical path. Prior to analysis particle size was reduced to <80 µm	85
Cu	Margarine	AE;ICP;L	Cu, Fe and Ni were determined following emulsification with Tween 80. The optimum margarine concentration in the emulsion was 35%	204
Fe	Water	AA;F;L	Fe, Mn and Zn LODs were 2.5, 0.68 and 0.24 µg l^{-1}, respectively, following preconcentration	344
Fe	Human milk, infant formula	AA;F;L	The development of an *in vitro* method to simulate new-born digestion and to study Fe and Zn bioavailability was carried out	345
Fe	Wine	AA;F;L	The cloud point phenomenon was used to determine free and tannin-bound Fe in wine. The LOD was 0.02 mg l^{-1}	236
Fe	Rum	EDXRF;-;L	See Cu, ref. 225	225
Fe	Table olives	AA;F;L	A standard method, for industry QC laboratories, was validated for the determination of Fe and Mn. The LODs were of 0.106 and 0.022 mg l^{-1}, respectively	346
Fe	Biscuits	AA;CV;L	Fortification with Fe and Mn was investigated in an unusual application of CVAAS	247
Fe	Margarine	AE;ICP;L	See Cu, ref. 204	204
Hg	Drinking water	AA;CV;FI	Hg was retained as Hg 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol in an on-line knotted reactor	248
Hg	Rice	AA;-;L	See Cd, ref. 363	363

Table 2 Analysis of foods and beverages (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Hg	Seafood	AA;CV;FI	The results of an interlaboratory trial were described	280
Hg	Biological RMs	AA;CV;HPLC	Samples were microwave oven digested using methanolic KOH, the digest cleaned up using CH_2Cl_2 and HCl and methylmercury quantified using HPLC-UV post column oxidation-CVAAS. The LOD was 10 μg kg^{-1}	157
Hg	Food RMs	AA;ETA;L	An *in-situ* concentration technique with a Pd Zr coating and a chemical modifier was described (modifier not given in abstract)	237
Hg	Food colours	AA;ETA;Sl	Slurries were prepared in 1% w/v Triton X-100 1% v/v HNO_3 2% w/v $KMnO_4$ 3% w/v $Ag(NO_3)_2$	238
Hg	Biological RM, seafood, shellfish	AE;MIP;cold trap	Methyl-, diethyl- and inorganic mercury were determined at LODs of 0.95, 6 and 1.25 ng l^{-1} using a method comprising microwave assisted extraction and a semi-automated capillary cold trap-MIP-AE spectrometer	155
Hg	Water	AE;ICP;FI	Hg was extracted as Hg 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol complex, at pH 9.2, mediated by micelles of polyethyleneglycol mono-*p*-nonylphenyl ether. The LOD for the FI-CV-ICP-AES system was 4 ng l^{-1}	220
Hg	Biological RMs	MS;ICP;CE	Inorganic, methyl- and ethylmercury were speciated using an on-line CE-ICP-MS system. The species were separated as Hg cysteine complexes. The construction and performance of the interface were described	156
I	Seafood	MS;ICP;L	3% NH_3 solution was added to digests (1 + 1, v/v) as stabiliser. Levels up to 12.7 mg kg^{-1} were found in fish samples	246
Li	Milk products, smoked fish	AA;F, air C_2H_2;L AA;F, N_2O C_2H_2;L	See Ca, ref. 336	336
Mg	Human milk, blood, urine, faeces	AE;ICP;L	See Ca, ref. 12	12
Mn	Water	AA;F;L	See Fe, ref. 344	344
Mn	Food	AA;F;L	4 surfactants and microemulsions were studied	205
Mn	Table olives	AA;F;L	See Fe, ref. 346	346
Mn	Biscuits	AA;CV;L	See Fe, ref. 247	247
Ni	Foods	AA;F;L	Ni was preconcentrated on-line using a minicolumn packed with Amberlite XAD-2 loaded with 2-(2-benzothiazolylazo)-2-*p*-cresol	233
Ni	Wheat flour	AA;ETA;Sl	See Cr, ref. 275	275
Ni	Margarine	AE;ICP;L	See Cu, ref. 204	204
P	Human milk, blood, urine, faeces	AE;ICP;L	See Ca, ref. 12	12
Pb	Water, tea CRM, herbal medicines	AA;F;FI	Pb was determined using a "multiplex" sample loading procedure, *i.e.*, 1 single large injection was separated into 8 smaller ones. The authors claimed this increased sample retention in a knotted reactor and offered the potential for improved LODs	222
Pb	Drinking water	AA;ETA;L	See Cr, ref. 224	224
Pb	Sunflower oil	AA;ETA;L	See Cd, ref. 215	215
Pb	Wine	AA;ETA;L	See Cd, ref. 241	241
Pb	Wine	AE;ICP;L	A Pb-quinolin-8-ol complex was formed on-line at pH 6.8, collected on a resin and then countercurrent eluted using HNO_3. Using a USN an LOD of 0.15 μg l^{-1} was obtained for a 10 ml sample of wine	224
Pb	Wine	PIXE;-;L	Samples, 5 ml, were concentrated below a halogen lamp, 8 μl aliquots transferred to a filter paper and Pb determined by PIXE. The LOD was approximately 50 ppb	251
Pb	Wine	MS;ICP;L	An interesting study, part of the International Measurement Evaluation Programme, showed considerable variability in results for Pb in wine. 129 laboratories participated and one third of results deviated by ±50% of the certified result. By contrast, all of 14 national measurement institutes reported results within ±10% of the certified value	257
Pb	Rice	AA;-;L	See Cd, ref. 363	363
Pb	Food colours	AA;ETA;Sl	See As, ref. 332	332
Pb	Raisins	AA;ETA;L	High Pb levels were found to be due to a contaminated copper fungicide	259
Pb	Foods	AA;ETA;Sl	See Cd, ref. 202	202
Pb	Cereals	MS;ICP;L	See Cd, ref. 341	341
Se	Mineral water	AA;Hy;L, AF;Hy;L	5 min enrichment on a gold wire yielded an LOD of 5 pg ml^{-1}	217
Se	Wine	AA;ETA;L	Ni and Sr were evaluated as chemical modifiers	240
Se	Human milk	AA;-;L	An interesting study explored the consequences of the Finnish decision to add Na_2SeO_4 to fertilisers. Direct analysis of milk samples found that supplementation had increased the Se level in maternal milk	269
Se	Rice	AF;Hy;L	Foliar application of Se resulted in fortification of Chinese rice by approximately 20-fold	347
Se	Rice	AF;Hy;L	A further paper on foliar application of Se. 30 rice products were analysed	348

Table 2 Analysis of foods and beverages (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Se	Mushrooms	AA;CV;HPLC	5 extraction procedures were considered and a 3-step process involving the use of H_2O extraction and 2 proteolytic enzymes pepsin and trypsin proved to be the most suitable for extracting Se	207
Se	Seafood	AA;ETA;L	Ultrasonic extraction and fast analysis by omission of the pyrolysis stage were used in an evaluation of "analytical minimalism"	209
Se	Seafood	AF;Hy;HPLC	Following protease lipase extraction and column clean up, Se was speciated using a continuous HPLC microwave-assisted digestion HG-AFS system	208
Se	Coffee	AE;ICP;HG	See As, ref. 333	333
Se	Dietetic compounds	AE;ICP;bromide generation	Volatile compounds of Se^{IV} and Se^{VI} were formed by reaction with Br^- in H_2SO_4 media in discontinuous mode and transported to the torch	249
Se	Oysters	MS;ICP;HPLC	Various extraction procedures, including enzymolysis, were discussed	206
Se	Oyster	-;-;-	See Cd, ref. 340	340
Se	Diets, food supplements, human plasma	-;-;-	The Se and Zn status of the New Zealand elderly female population was investigated. The results lead the authors to speculate that Se and Zn rich foods or nutritional supplements may be beneficial	80
Se	Brassica	MS;ICP;HPLC MS;ES;HPLC	The role of plants in phytoremediation was investigated	201
Se	Nuts	MS;ICP;HPLC	Se was speciated in Brazil, pecan, cashew and walnuts. The main species found was Se-methionine	349
Se	Yeast extracts	MS;ICP;L MS;ES;L	Sequential SEC, anion-exchange and cation-exchange LC allowed 30 Se species to be identified	229
Se	Yeast	MS;ICP;ETV	Se-containing proteins were separated by SDS-PAGE, then the bands removed and Se determined by ETV-ICP-MS	318
Sr	Wine	MS;ICP;L	^{86}Sr:^{87}Sr analysis using multicollector-ICP-MS discriminated wines by their geographic origin	245
Sr	Milk products, smoked fish	AA;F, air C_2H_2;L AA;F, N_2O C_2H_2;L	See Ca, ref. 336	336
Th	Foods	MS;ICP;L NAA;-;-	Daily Pakistani dietary intakes were calculated	350
Tl	Wine	AA;ETA;L	Following digestion with HNO_3 H_2O_2, Tl was treated with KI and extracted into IBMK, yielding an LOD of 0.05 $\mu g\ l^{-1}$	226
U	Water	MS;ICP;L	3 different analytical techniques were compared	279
U	Wheat	MS;ICP;L	Wheat samples from 10 regions of Saudi Arabia were analysed	351
Zn	Water	AA;F;L	See Fe, ref. 344	344
Zn	Human milk, infant formula	AA;F;L	See Fe, ref. 345	345
Zn	Human milk, cow's milk infant formula	AA;-;-	See Cu, ref. 343	343
Zn	Rum	EDXRF;-;L	See Cu, ref. 225	225
Zn	Diets, food supplements, human plasma	-;-;-	See Se, ref. 80	80
Zn	Foods	AF;Hy;L	The advantages of HG from the organised medium of cetyltrimethylammonium bromide were contrasted with that from aqueous media	232
Zn	Bovine offal, muscle	AA;ETA;L	See Cd, ref. 199	199
Zn	Oyster	-;-;-	See Cd, ref. 340	340
Various (5)	Water	AA;ETA;L	As, Cu, Mn, Sb, and Se were simultaneously measured using Zeeman-effect ETAAS	242
Various (5)	Camel, cow, human milk, infant formula	AA;-;L	Camel, cow and human milk was collected in Kuwait and infant formulae purchased locally. Cu, Fe, Mn, Se and Zn were determined. Camel's milk contained 4 10-fold and 7 20-fold, respectively, more Fe and Mn than the other sample types	272
Various (6)	Goats' milk	AA;ETA;L AA;F;L	Cd, Cu and Pb were determined by ETAAS and Ca, Mg and Zn by FAAS in samples of Czech goat's milk	352
Various (4)	Cows' milk	AE;ICP;L	Ca, Fe, Mg and Zn were either determined following microwave assisted digestion or after sequential treatment with TCA then pepsin. The latter method allowed study of metal protein interactions	273
Various (26)	Infant formula	AE;ICP;L	Analysis of supermarket samples from the USA, UK and Nigeria was conducted following microwave digestion. The EU drinking water maximum admissible concentrations for Al and Ba and the US EPA standard for Tl were violated in some infant formula brands	271
Various	Wine	MS;ICP;L	Semi-quantitative and quantitative analysis were compared	353
Various (4)	Milk powder	MS;ICP;L	Ultrasonic slurry sampling ETV reaction cell ICP-MS was used to determine Cd, Cr, Pb, Zn at LODs of 0.2, 3, 2 and 37 ng g^{-1}, respectively	244
Various	Food, beverages	-;-;-	A review, with 150 references, of papers addressing the issue of authenticity	354
Various (4)	Mushrooms	AA;-;-	A survey of Cd, Cu, Hg and Pb in the area around a Slovakian smelter found very high concentrations, including Hg at up to 71 mg kg^{-1} dry weight	355

Table 2 Analysis of foods and beverages (*continued*)

Element	Matrix	Technique; atomization; presentation[a]	Sample treatment/comments	Ref.
Various (4)	Game	AA;F;L	As, Cd, Hg and Pb were determined in tissues from pigs, roes and deer. Pb content exceeded food regulations in 25% of cases. Although not stated in the (Polish) abstract, one may speculate that the Pb originated from the means of slaughter	356
Various (8)	Wheat and rye	AA;F;L	Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb and Zn in Swedish samples were measured over a 15 year period	274
Various (5)	Mushrooms	AA;-;L	The levels of Cd, Cu, Fe, Mn, and Zn were surveyed in Croatian mushrooms	357
Various (11)	Seafood CRMs	AA;F;L,Sl AA;ETA;L, Sl	Classical pre-treatments such as microwave assisted-acid digestion and slurry techniques were compared with microwave energy or ultrasound energy assisted-acid leaching process and enzymatic hydrolysis methodologies based on the use of pronase E (As, Cd, Cr, Cu, Fe, Mg, Mn, Ni, Pb, Se, Zn)	358
Various (5)	Fresh eggs	AA;F;L AA;ETA;L	Cu, Pb and Zn were determined using Y Pd citric acid as chemical modifier and a Zeeman-effect ETAA spectrometer. Ca and Mg were measured using FAAS	359
Various (6)	Foodstuffs	AA;ETA;L	As part of a chromium intake study, Ca, Fe, K, Mg, Na and Zn were also determined	264
Various	Wheat flour, bread	AE;ICP;L	Analysis of Bulgarian flour and bread yielded the recommendation that they should be fortified, due to the low levels of micronutrients detected in the samples studied	360
Various	Honey	PIXE;-;- TXRF;-;-	Trace elements were measured in Polish honey	361
Various (19)	Herbs and herbal infusions	MS;ICP;L AA;F;L	As, Ba, Ca, Cd, Co, Cr, Cu, Fe, Li, Mg, Mn, Ni, Pb, Se, Sn, Sr, Ti, V and Zn were measured	362
Various (11)	Diets, breast milk, infant formula	MS;ICP;L	A longitudinal 6-day duplicate diet study for pregnant and non-pregnant subjects showed low intakes of Cu, Fe and Zn for Australian infants and "migrants" (Ba, Ca, Cu, Fe, K, Mg, Na, P, Pb, Sr, Zn)	263
Various (15)	Foods	MS;ICP;L	A method for the routine determination of Al, As, Cd, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, Se, Sn, V and Zn was based on microwave assisted digestion and quadrupole ICP-MS. Utilising mathematical interference correction and QC procedures the method was proposed for high throughput laboratories	243
Various	Lobster	MS;ICP;L	Soxhlet, room temperature mixing, sonication, microwave assisted, supercritical CO_2 and subcritical H_2O extractions were evaluated for a variety of solvent systems and optimum conditions determined	112
Various	Biological and clinical samples, foods and beverages	-;-;-	A comprehensive review of annual developments in the determination of the cited samples by atomic spectrometry	1
Various	Foods, clinical samples	AMS;-;-	The potential for AMS in nutrition research was discussed	35

[a]Hy indicates hydride and S, L, G and Sl signify solid, liquid, gaseous or slurry introduction, respectively. Other abbreviations are listed elsewhere.

> 2900 μg l^{-1}. One-third of the results were below −50% or above +50% of the certified concentration: 40% of participants reported to within ±10% uncertainty. Three sets of results from the NMKL Interlaboratory Study were reported in our last Update[1] and a further study has since appeared.[280] Ten laboratories took part in this work on the measurement of Hg in seven seafood products by FI-CVAAS. The sample concentrations and analytical repeatability and reproducibility were reported.

3 Conclusions

One of the principal features of recent Updates has been the steady progress in *in vivo XRF determination of lead in bone* to the point where now, for any study involving Pb exposure, data on XRF measurements of Pb in bone seem almost mandatory (see sections 1.3.3.3 and 1.9.11). But are these measurements precise and accurate? In a noteworthy collaboration between physicists and chemists, results by XRF measurement have been compared with those obtained by digestion of bone samples and measurement by ETAAS.[48–51] The ETAAS measurements[281] showed that the surface tibia Pb measurement was greater than the core concentration by about 5–8 μg g^{-1}. Measurements by ^{109}Cd-based K-shell XRF agreed well with the surface Pb concentration by ETAAS.[50] Thus, the XRF measurement reflects the Pb concentration at the surface of the tibia rather than at the core. With L-shell XRF using an X-ray generator as a source, results were a cause for concern.[51] Although overall the agreement between L-shell XRF and ETAAS measurements was good, the variability of the XRF measurement was unacceptably high. For intact leg measurement, the measurement uncertainty exceeded the concentration in almost all cases. The range of applications involving XRF has steadily increased in recent years and now includes many different tissues and body fluids, honey and alcoholic drinks (Tables 1 and 2).

New findings have emphasized the importance of *selenium in nutrition* and increased concern for those areas in the world where Se depletion is found. Of great significance is the finding by Brooks *et al.*[282] that low plasma Se levels in elderly men are associated with a 4–5 fold increased risk of prostate cancer. This is further evidence for the role that dietary Se has in the prevention of prostate cancer, dramatically shown in the double-blind cancer prevention trial reported by Clark *et al.* in 1998, in which a daily supplement of 200 μg Se was associated with a 63% reduction in the incidence of prostate cancer.[283] Selenium also appears to detoxify Hg released from amalgam fillings. Patients who claim symptoms of ill heath from fillings have significantly lower blood Se concentrations than those with fillings but no ill effects.[75] Correlations are also seen in tissues between Hg and Se concentrations.[21] Tan *et al.*[183] suggested that Se supplements should be given in pregnancy, as they had found significantly

lower plasma Se in pregnant women with impaired glucose tolerance or with gestational diabetes mellitus than in normal pregnant women. There is also an indication that low Se status may be associated with miscarriages.[182]

Having drawn attention in the last Update to the effects of organic production of foods on their trace element concentrations, it is apparent that interest is being maintained in this topic and there may also be work in the future involving genetically modified foods. Other new *developments highlighted in the last year or so* included the methylated As^{III} species that appear to be formed during the metabolism of inorganic As. Studies to further elucidate the mechanisms involved have been reported during this current review period. After a lull period for a couple of years there is renewed interest in the tungsten-coil atomiser.

An analytical challenge has been *the determination of uranium and the actinides in biological samples*, now achieving greater prominence because of the interest in the exposure to depleted uranium of military personnel[190] and aid workers[189] in the aftermath of the wars in Kuwait and Kosovo. Determination may be made by quadrupole ICP-MS[189] which is quicker and more straightforward than determination by α-spectrometry, but sector-field ICP-MS offers superior sensitivity.[27]

One other topic that shows considerable recent development is the use of permanent chemical modifiers for ETAAS. Several reports have mentioned the advantages of using reagents that require just a single application to the furnace. Solutions of Rh and W are particularly favoured and look likely to increase in popularity; our next Update should reveal whether this is a real improvement or merely another fashion.

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